

Introduction to computational neuroscience : from single neurons to network dynamics



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slides : on the moodle or <https://biomedicale.u-paris.fr/~mgraupner/teaching.php> - michael.graupner@u-pariscite.fr

Lecture outline :

Introduction to Computational Neurosciences

1. Introduction (today) :

- A couple of (fun) brain questions

2. The Neuron (today) :

- Hodgkin-Huxley model
- Integrate-and-Fire model
- Rate model
- Cable theory

3. Neural networks (next course) :

- Rate models
- Spiking neuron models
- Examples

What's the brain good for ?



Tree
no neurons

C.elegans
302 neurons

Fly
1 000 000 neurons

Rat
50 000 000 neurons

Human
80 000 000 000 n.

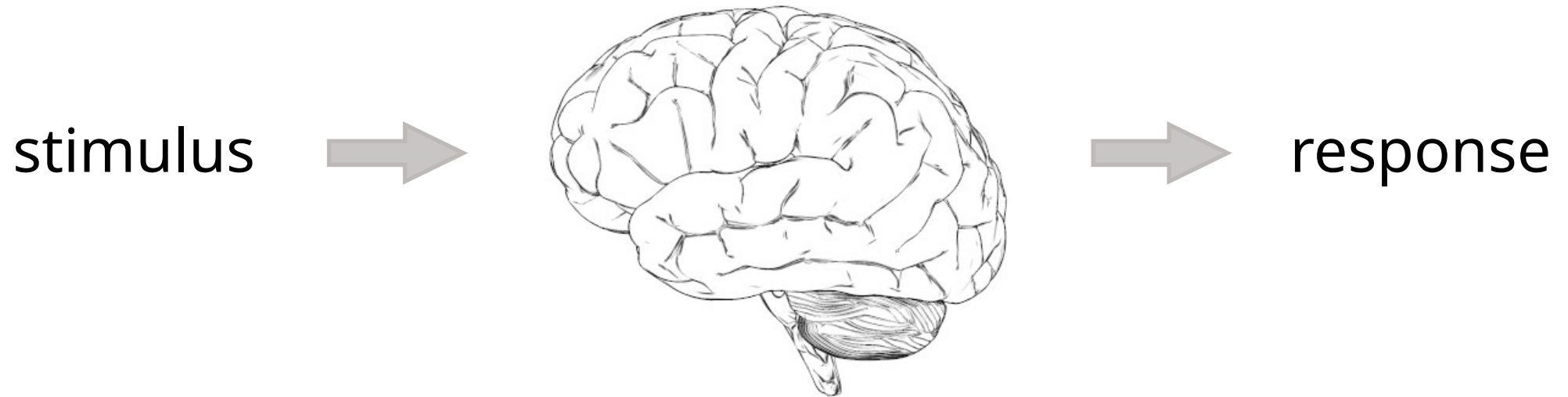
The brain generates motion
(=behavior)

more complex brains
generate a greater
variety of behaviors

more complex brains
can learn more
behaviors



Cognitive processing



What's the brain good at ?

			
chess	1	:	0
scrabble	1	:	0
Jeopardy!	1	:	0
video games	1	:	0
Go	1	:	0
Object recognition	1	:	1

Computers outperform humans in algorithmic tasks and tasks involving database mining.

What's the brain good at ?

Lionel Messi – Barcelona : Getafe CF 2007



What's the brain good at ?

RoboCup 2016

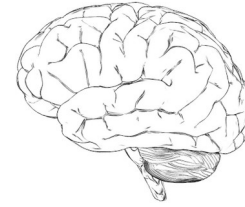


What's the brain good at ?

Boston Dynamics

<https://www.youtube.com/watch?v=tF4DML7FIWk&t=7s>

What's the brain good at ?



soccer

0

:

1

numerous
motor
tasks

0

:

1

(it's getting tight)

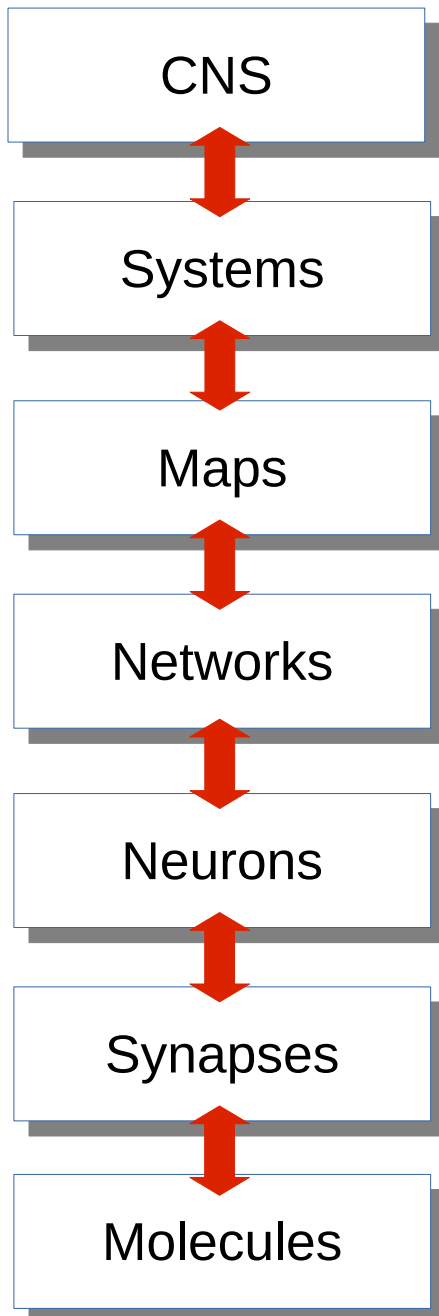
Brains are better in tasks involving interactions with the real world.

Why model the brain ?

- to understand it
- to repair/improve it
- to get inspired

What makes
understanding/
modeling the
brain so complex?

The many spatial scales of the brain



1 m

10 cm

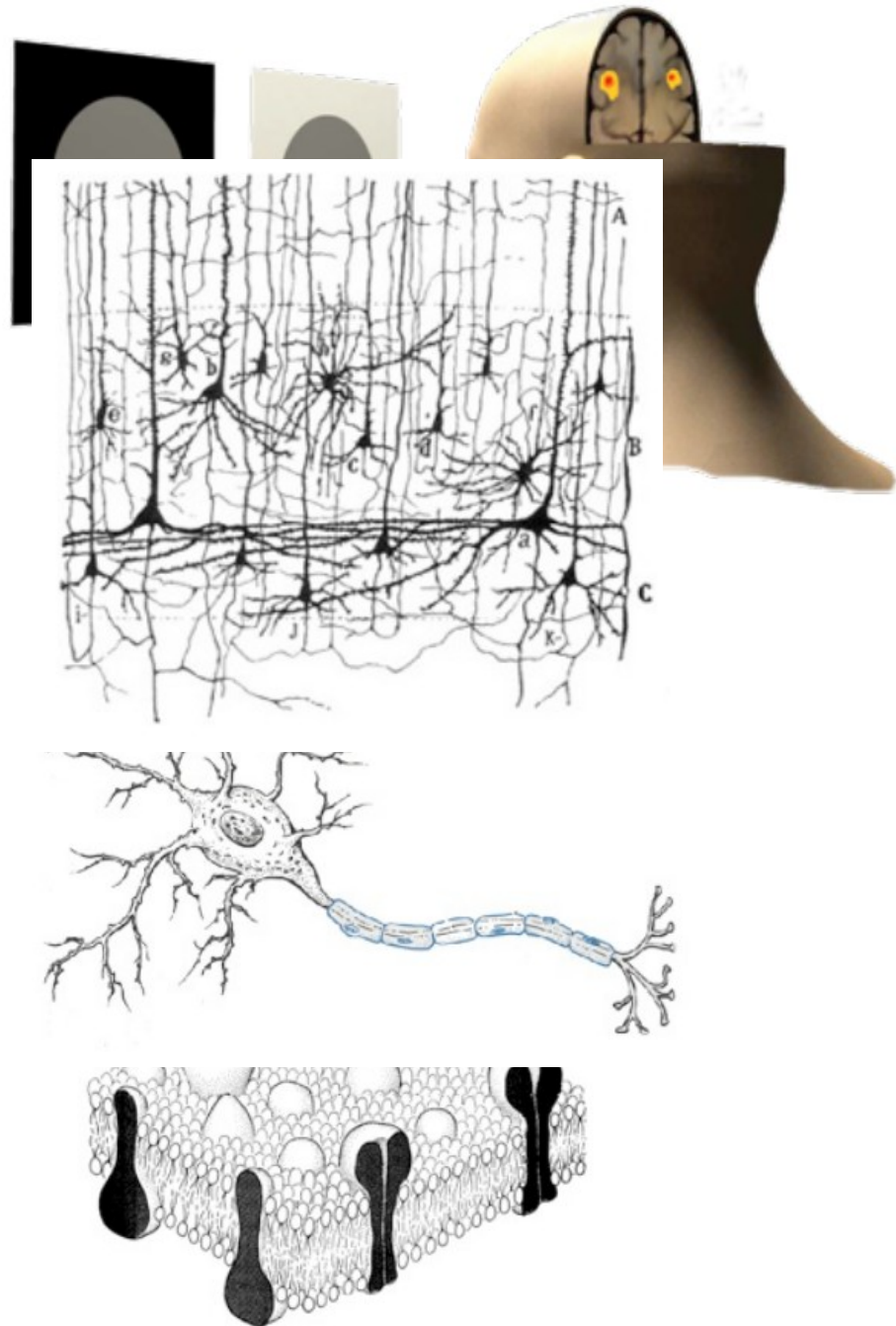
1 cm

1 mm

100 μ m

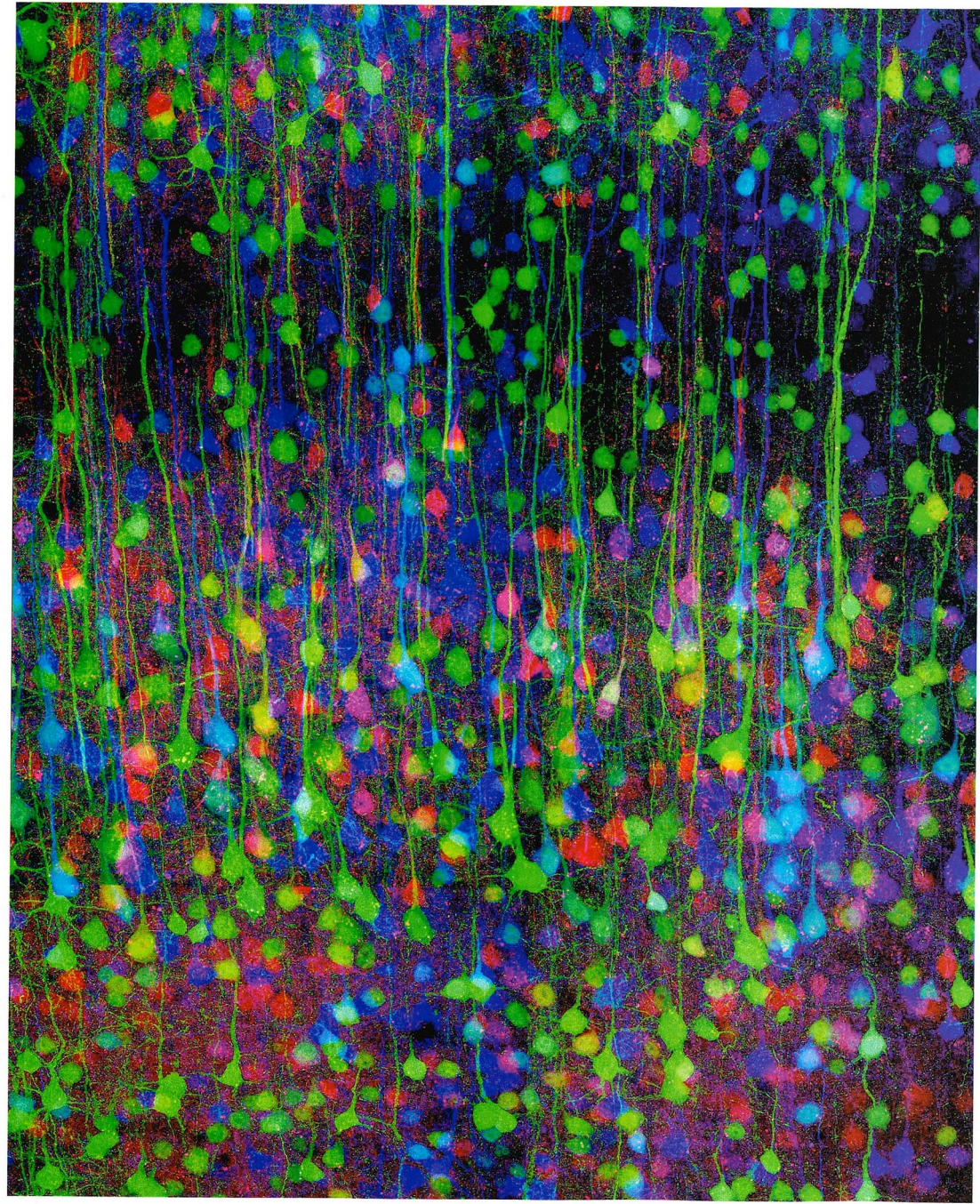
1 μ m

1 nm



The large number of elements

86,000,000,000 neurones in
the human brain



[Nick Steinmetz, University of Washington]

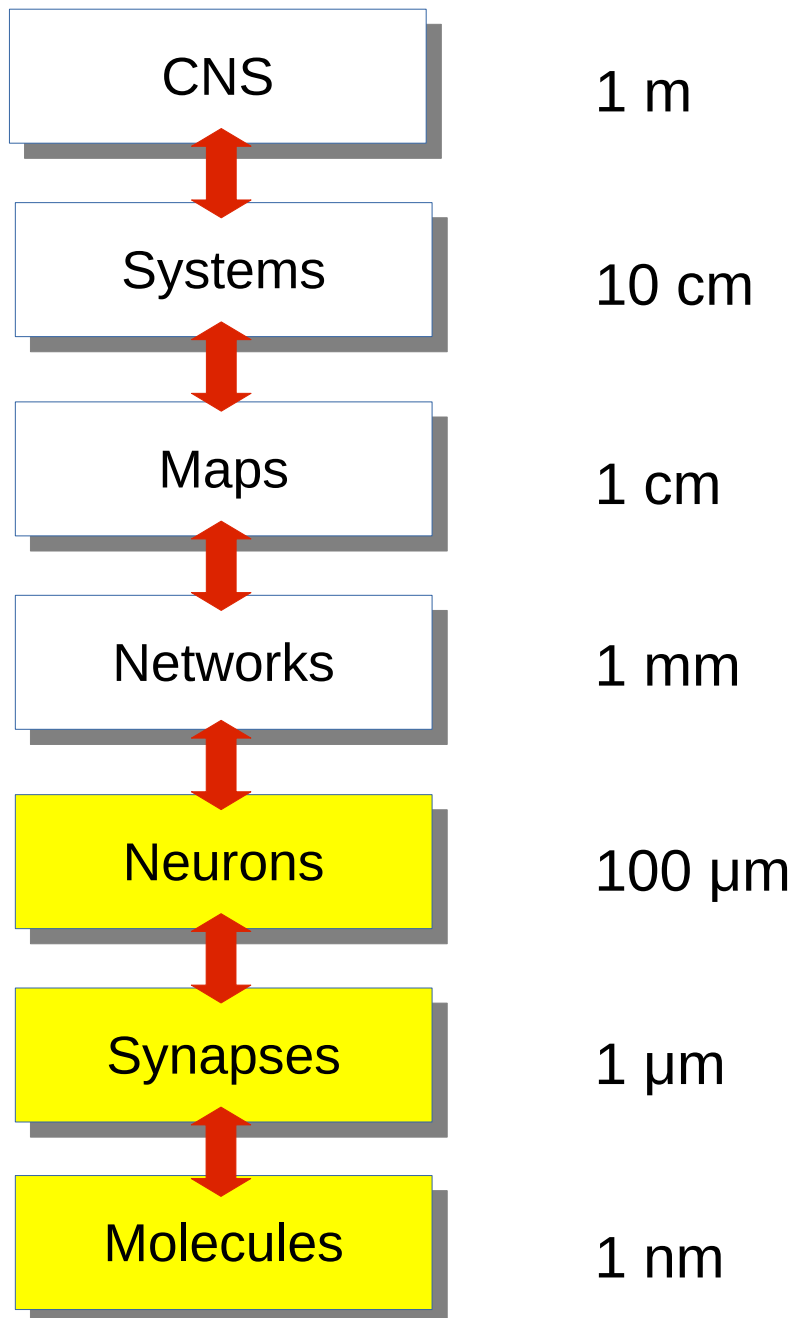
How does the
brain work ?

A physics/engineering approach

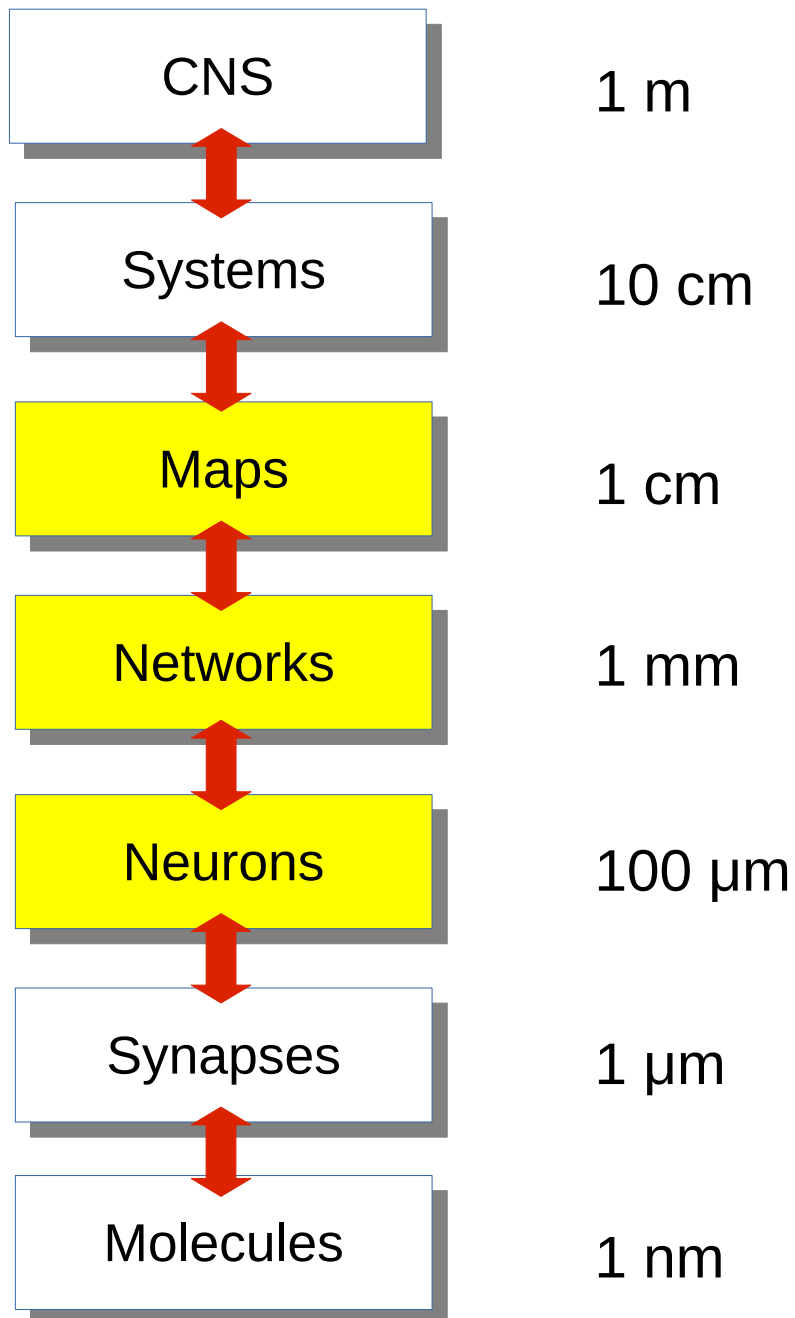
just rebuild the whole thing

→ reverse engineering the brain

The quest for mechanisms : Constructing the systems from parts



The quest for mechanisms : Constructing the systems from parts

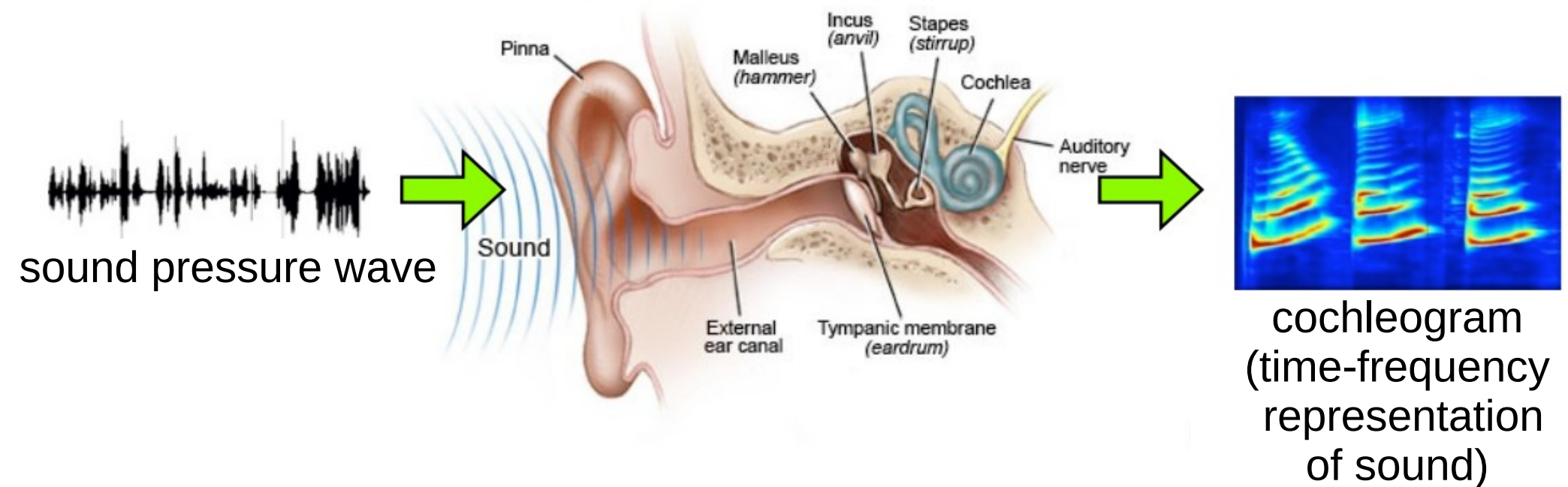


A computer science approach

Study the computational
problems

Computation : transforming and representing information

Normal hearing



Representation of information

Music example : Art Blakey – Mayreh



Representation of information more or less lossy

How to transmit the music of a jazz concert :

- Partition



- Sound



- CD



- Language

The other day, I went to this cool jazz concert ...



Why represent information differently

Example : numbers, twenty-three

XXIII

Roman system

23

Decimal system

00010111

Binary system

Why represent information differently

Example : numbers, twenty-three

XXIII

in ... ?

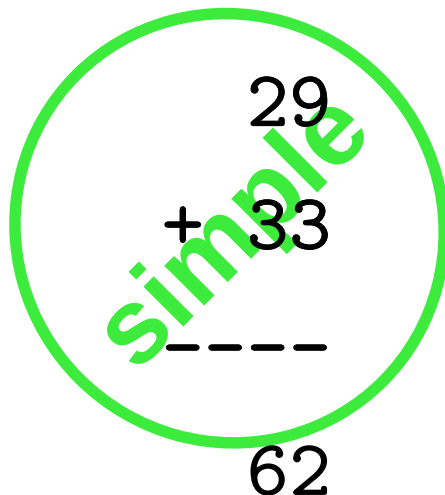
23

in multiples of 10

00010111

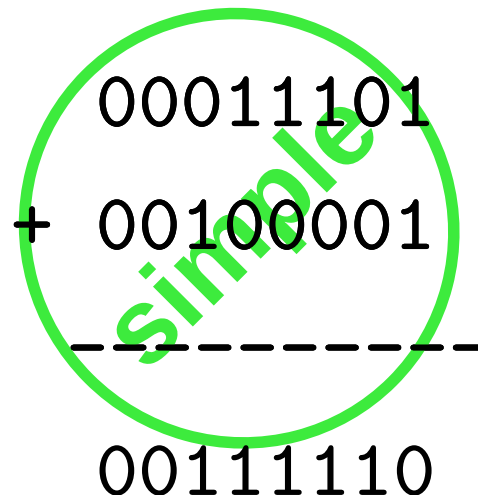
in multiples of 2

Can you add these number ?



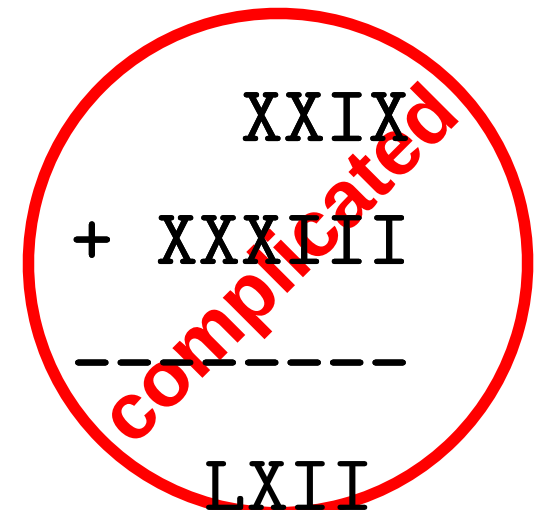
A green circle containing a simple addition problem. The numbers 29 and 33 are stacked with a plus sign between them. A dashed line is below the numbers, and the result 62 is written below the line. A green diagonal watermark reading "Simple" is overlaid on the circle.

$$\begin{array}{r} 29 \\ + 33 \\ \hline 62 \end{array}$$



A green circle containing a binary addition problem. The binary numbers 00011101 and 00100001 are stacked with a plus sign between them. A dashed line is below the numbers, and the result 00111110 is written below the line. A green diagonal watermark reading "Simple" is overlaid on the circle.

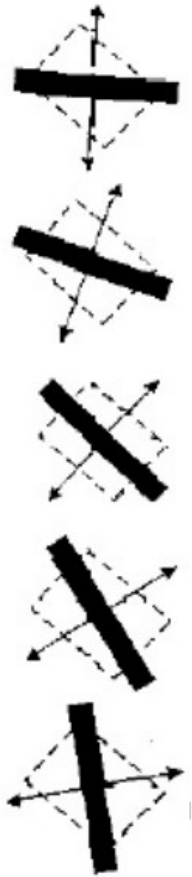
$$\begin{array}{r} 00011101 \\ + 00100001 \\ \hline 00111110 \end{array}$$



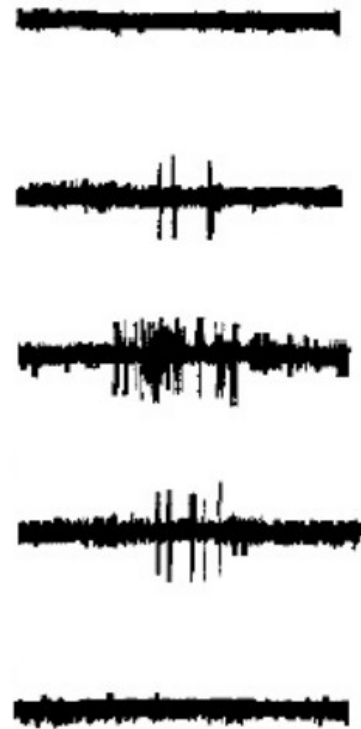
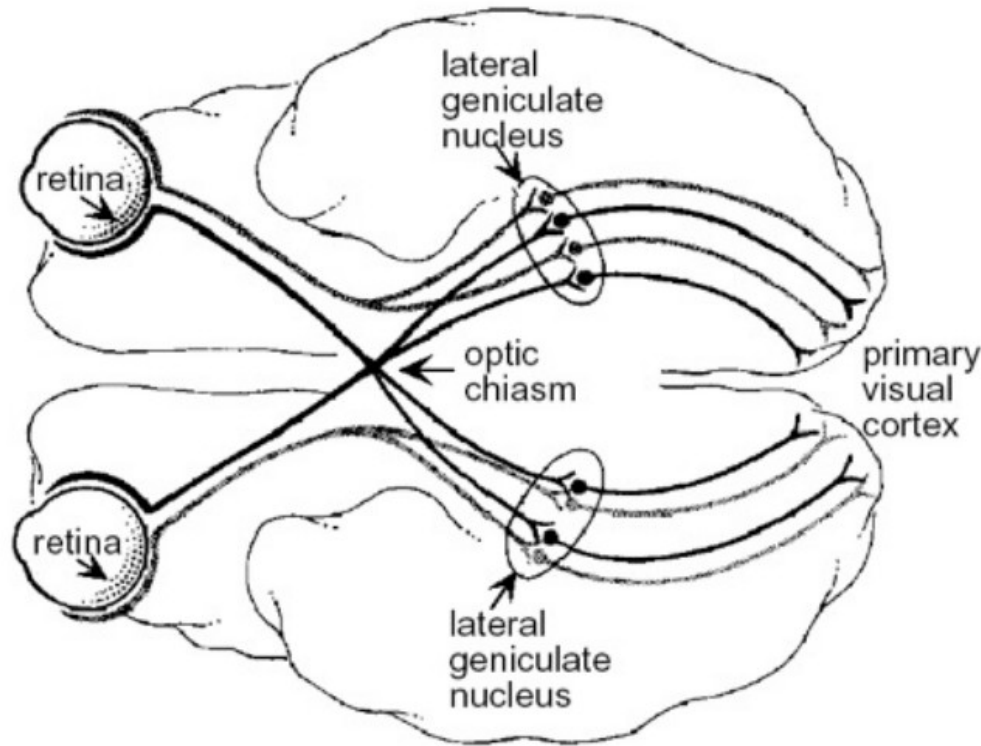
A red circle containing a Roman numeral addition problem. The Roman numerals XXIX and XXXIII are stacked with a plus sign between them. A dashed line is below the numbers, and the result LXII is written below the line. A red diagonal watermark reading "Complicated" is overlaid on the circle.

$$\begin{array}{r} XXIX \\ + XXXIII \\ \hline LXII \end{array}$$

Most famous example “edge detectors” in visual cortex



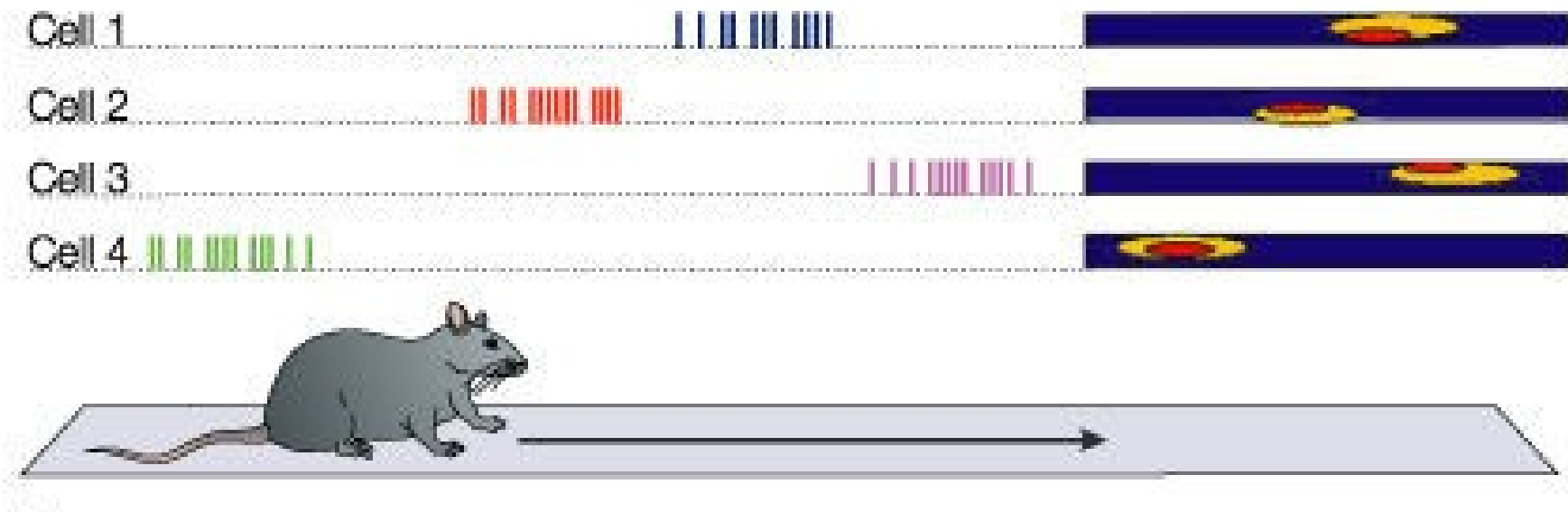
stimulus:
black
bar



Activity of
neuron in
visual cortex
(V1)

Another famous example “Place cells” in the hippocampus

Linear track



Another famous example “Place cells” in the hippocampus



What we understand

very little



What is required

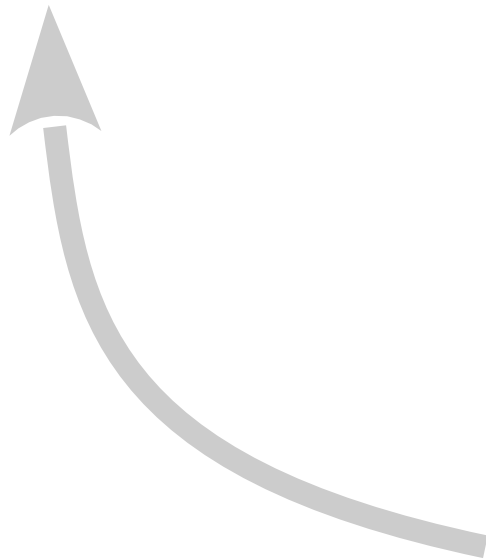
biologists, psychologist

- to probe the brains of animals and humans
- to design and carry out clever experiments
- to investigate and quantify human and animal behavior



physicists, computer scientists, engineers

- to formulate mathematical theories of information processing
- to create biophysical models of neural networks



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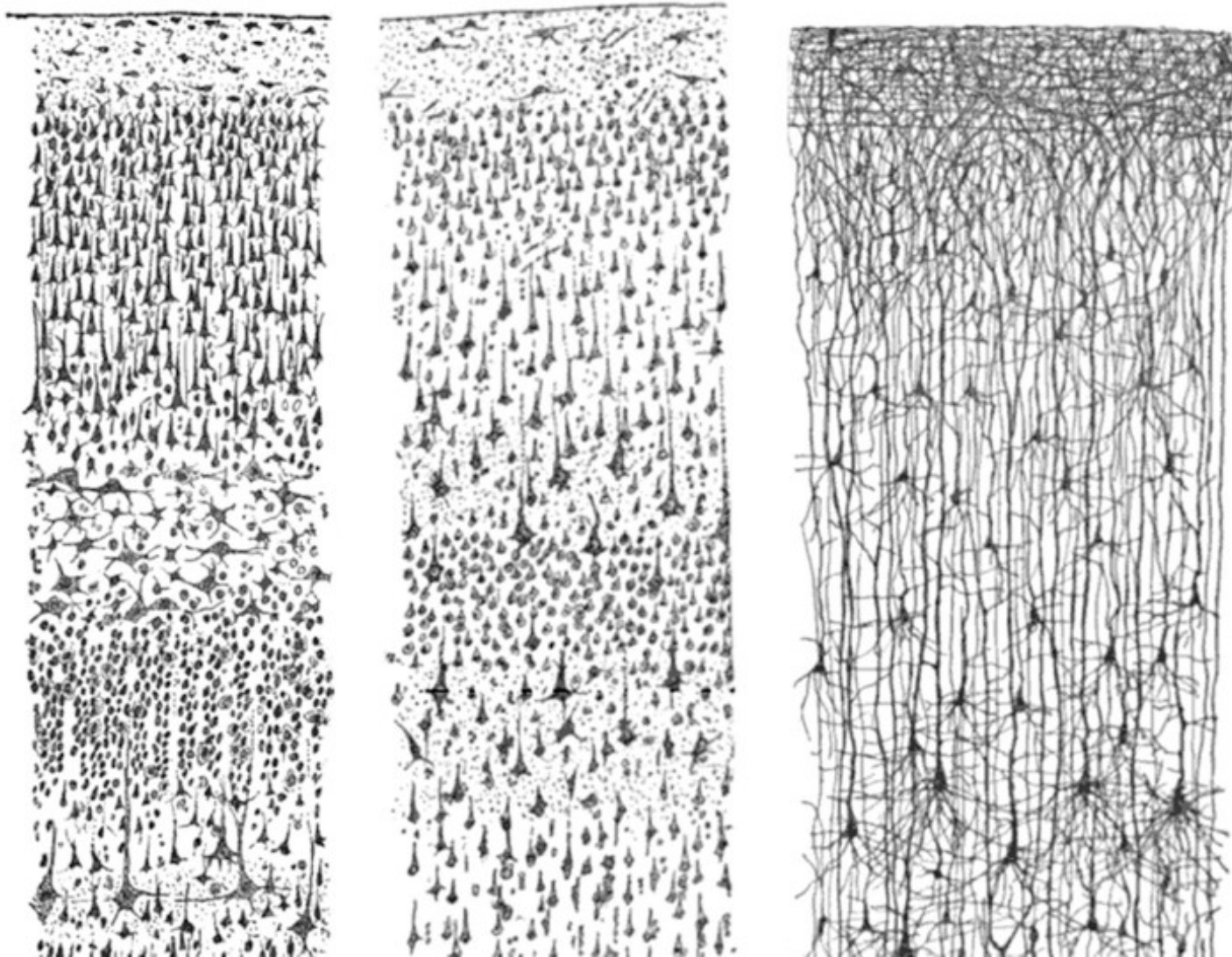
2. The Neuron (today) :

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- Rate model
- Cable theory

3. Neural networks (next week) :

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- Examples

What does the hardware look like ?



Ramon y Cajal (Nobel Prize 1906)

Joseph von Gerlach (1871), Camillo Golgi

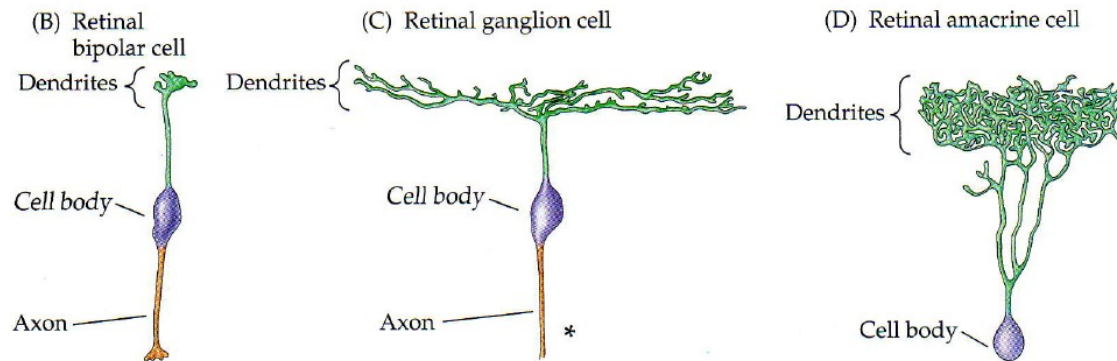


neuron doctrine



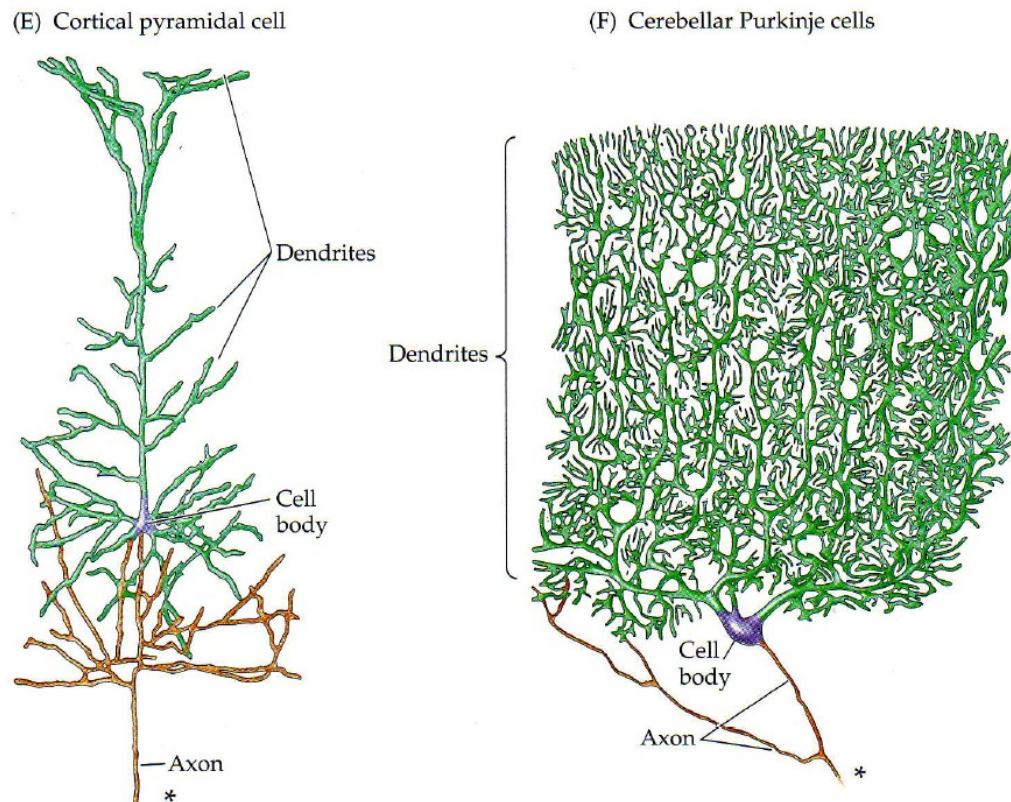
~~Reticular theory~~

Neurons = basic units of computation



Dendrites

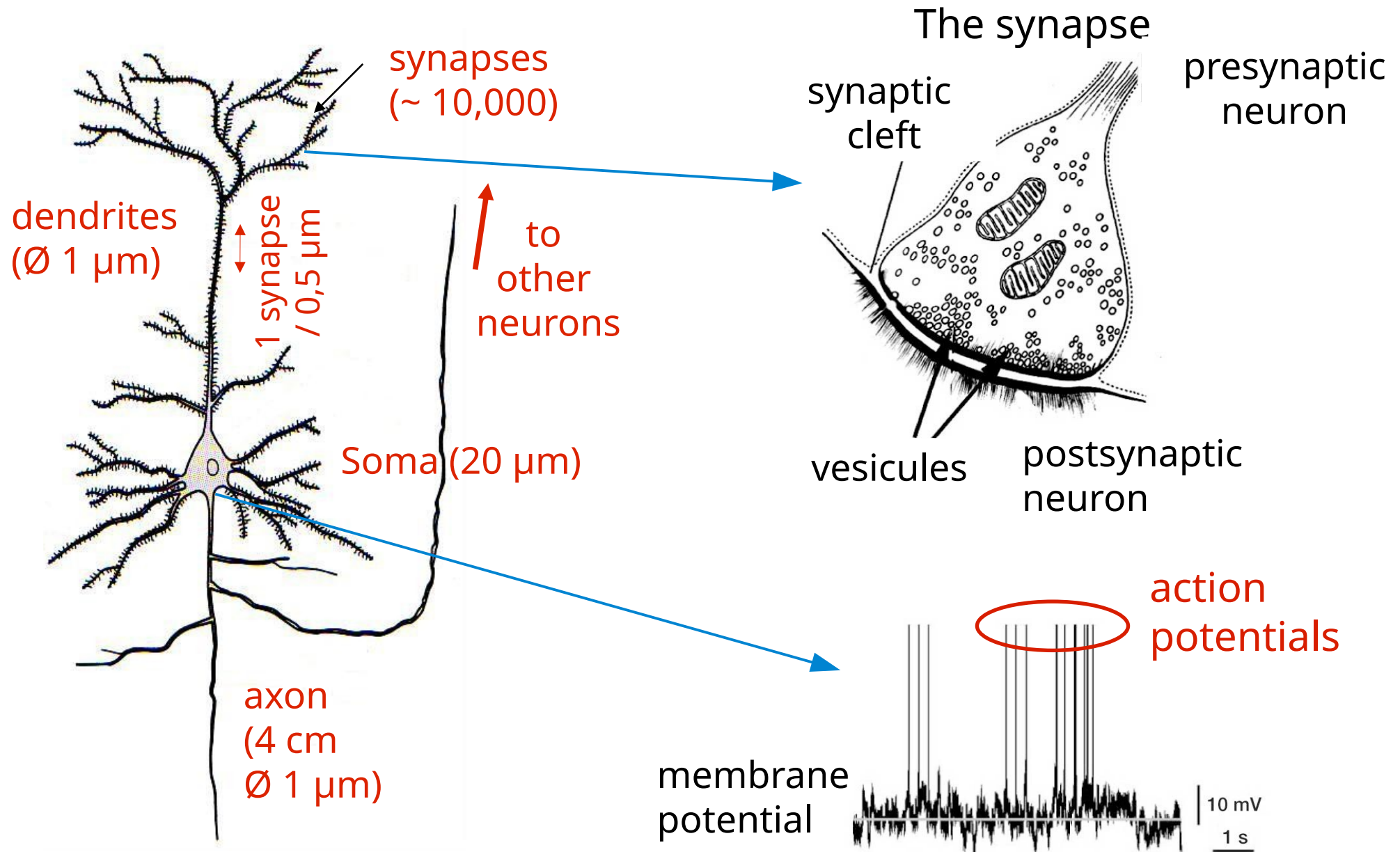
Soma



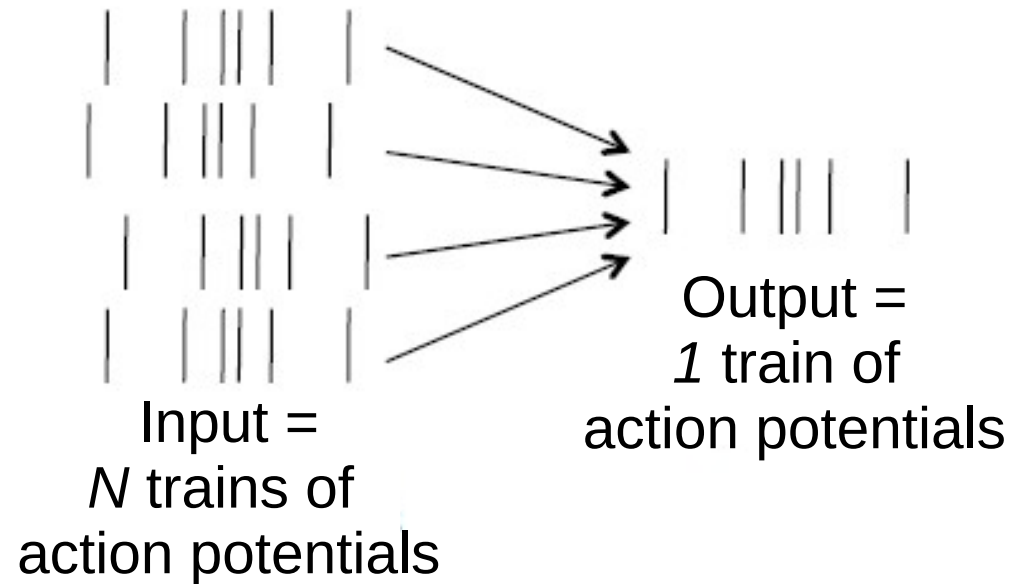
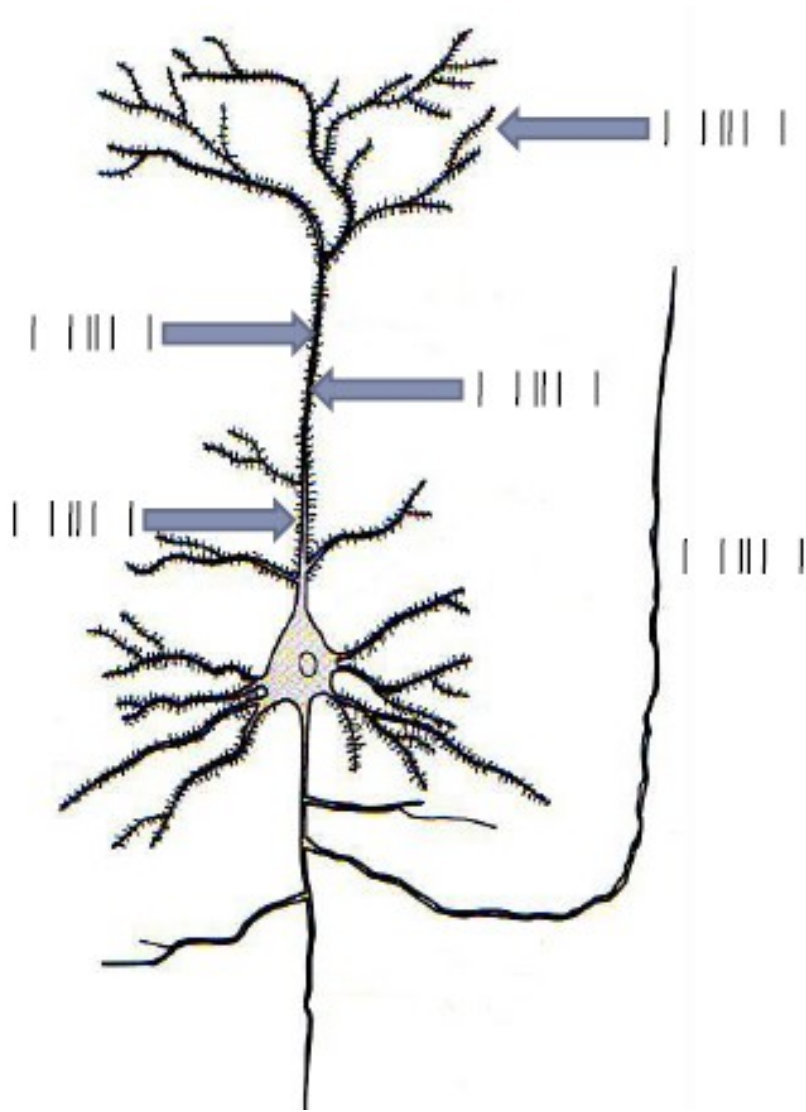
Axon

information flow

The typical cortical neuron



Neural integration



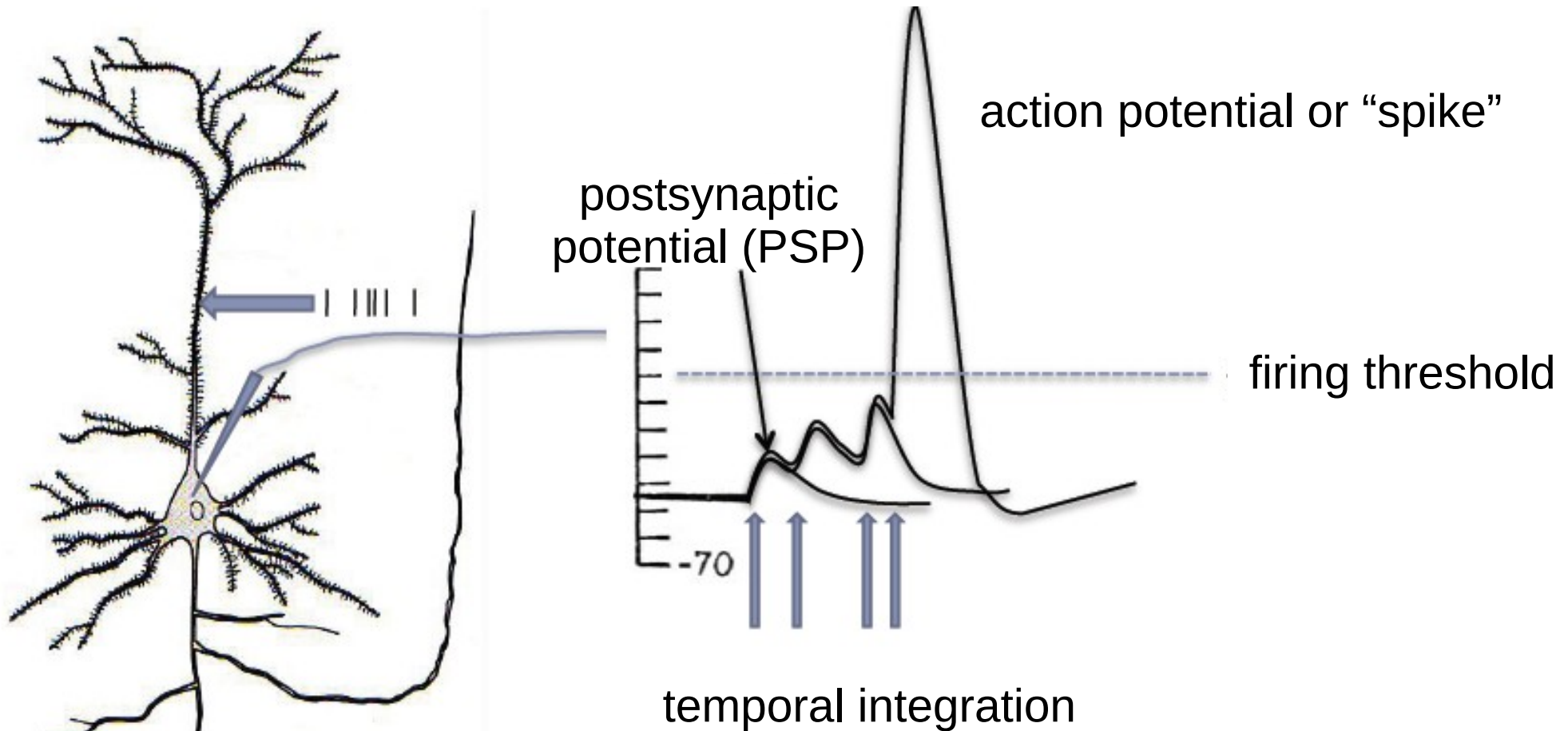
Synaptic current of one specific synapse (ij) :

$$I_s = G_{max} \Delta V \alpha(t) = w_{ij} \alpha(t)$$

Total synaptic current in neuron i at time t :

$$I_{syn}^i(t) = \sum_j w_{ij} \sum_k \alpha(t - t_j^{(k)})$$

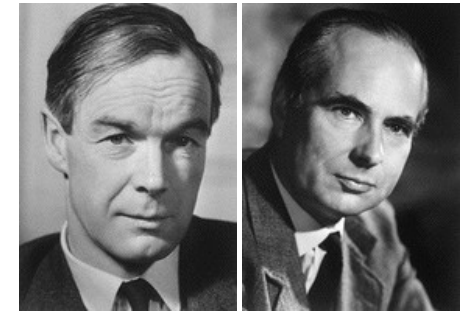
Neural integration



$$I_{syn}^i(t) = \sum_j w_{ij} \sum_k \alpha(t - t_j^{(k)})$$

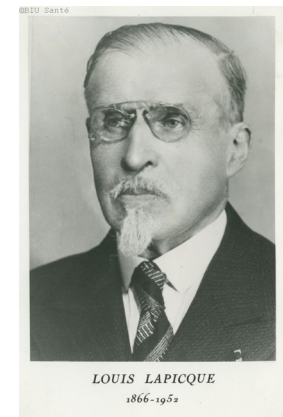
Single neuron models

- **Hodgkin Huxley model** : description of ion channel dynamics (Hodgkin & Huxley, 1952)
- **integrate-and-fire model** : description of input integration membrane potential dynamics (LaPicque, 1907)
- **rate model** : description of the mean firing rate dynamics
- **cable theory** : description of input propagation along the dendrites (Rall, 1962)



Hodgkin

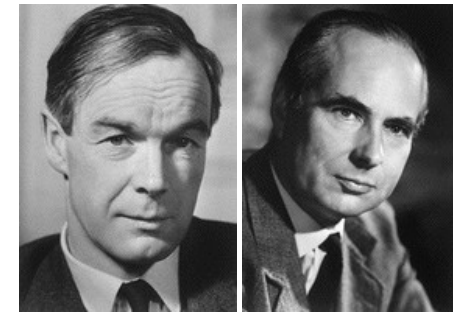
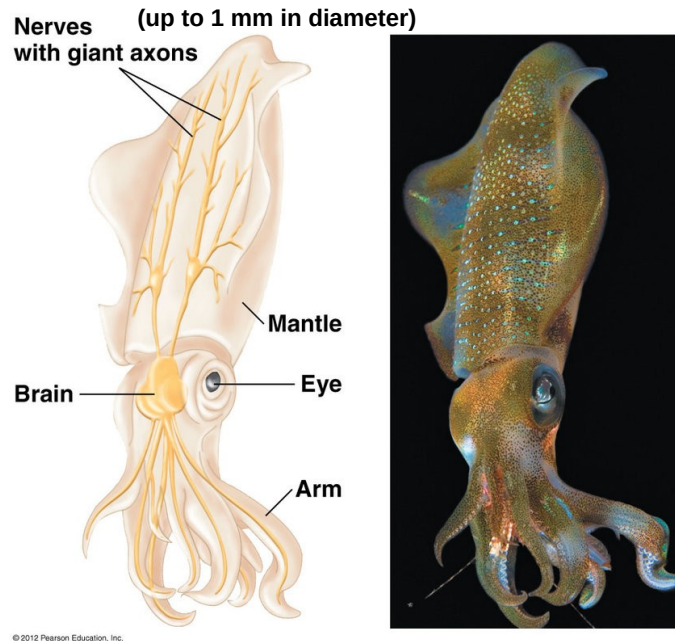
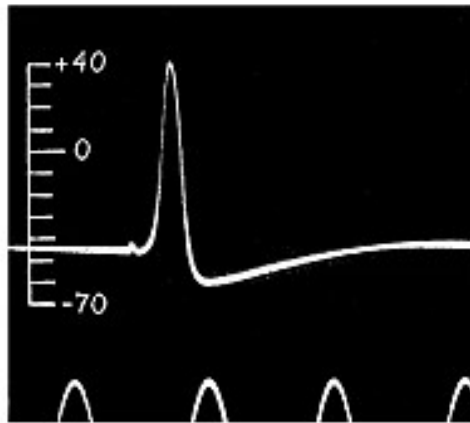
Huxley



Wilfrid Rall

Significance of the Hodgkin-Huxley model

- Hodgkin and Huxley performed first intracellular recording of an action potential

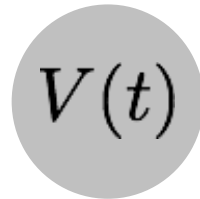
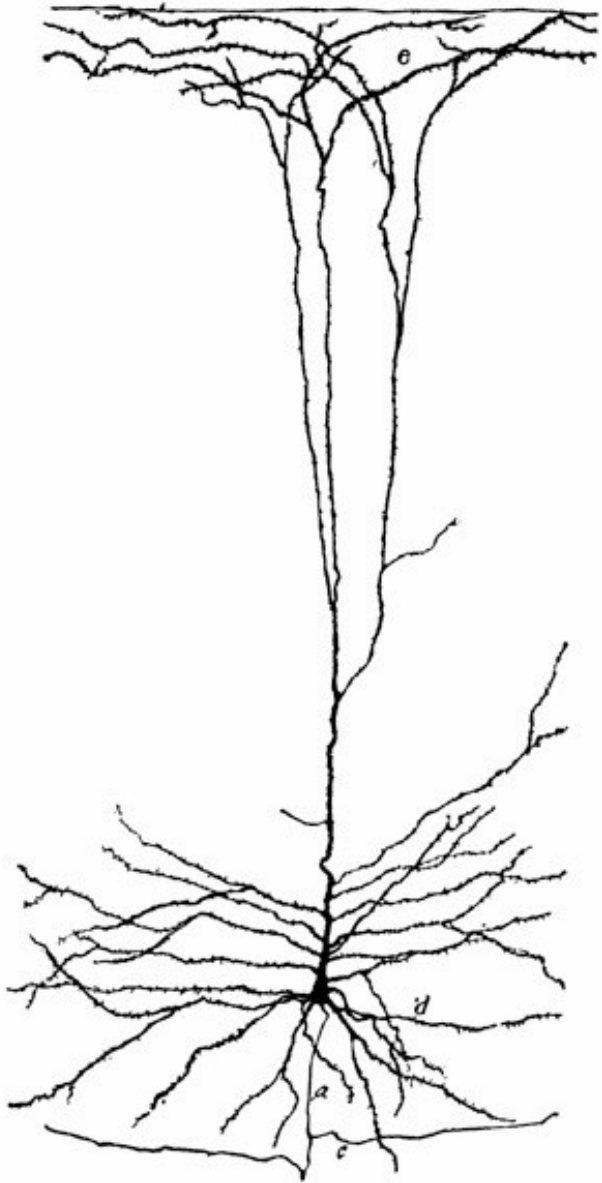


Hodgkin

Huxley

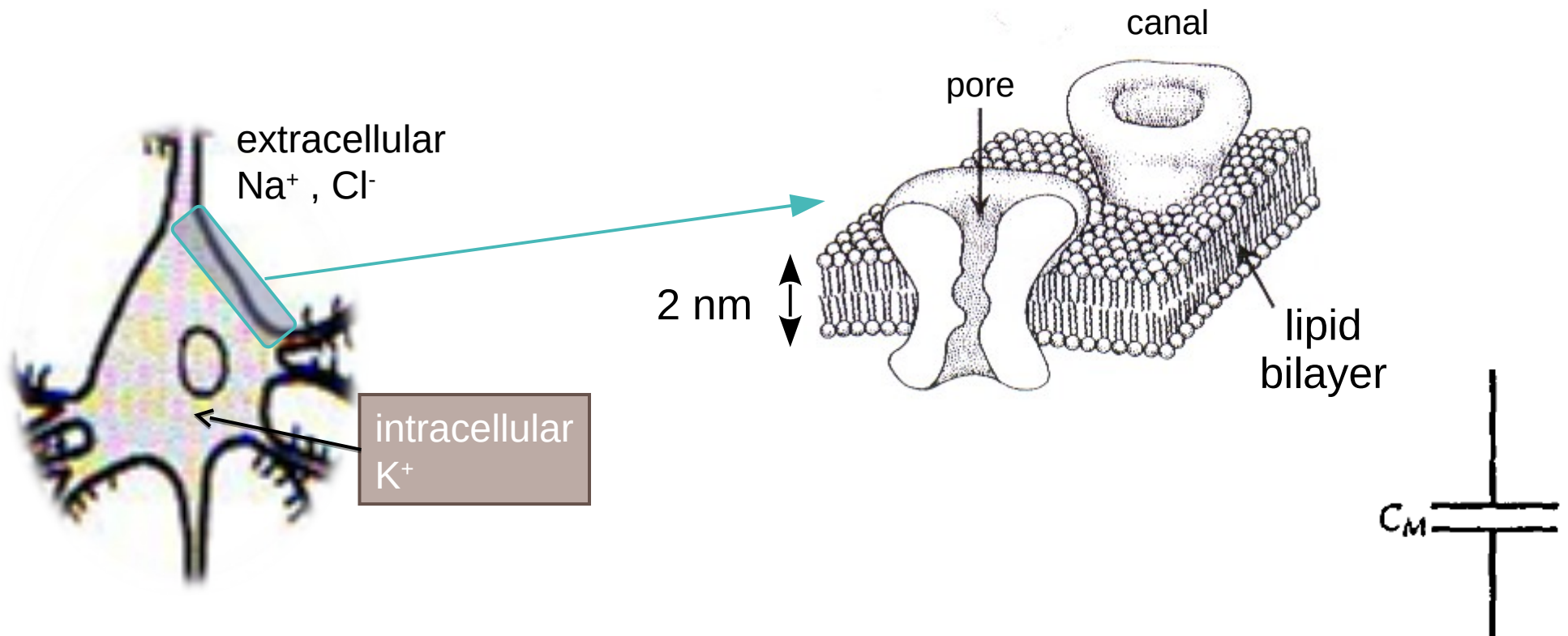
- using voltage-clamp protocol : demonstrated that two independent currents are underlying action potential – sodium and potassium
- empirical representation of the experimental data in a quantitative model : the Hodgkin-Huxley model -> links the microscopic level of ion channels to the macroscopic level of currents and action potentials

Simplified single neuron : single compartment model



The membrane

- Lipid bilayer (= capacitance) with pores (channels = proteins)



specific capacitance $1 \mu\text{F}/\text{cm}^2$
total specific capacitance = specific capacitance * surface

Physics reminder

Ohm's law :

The current flowing through a resistor is directly proportional to the voltage drop across the resistor.

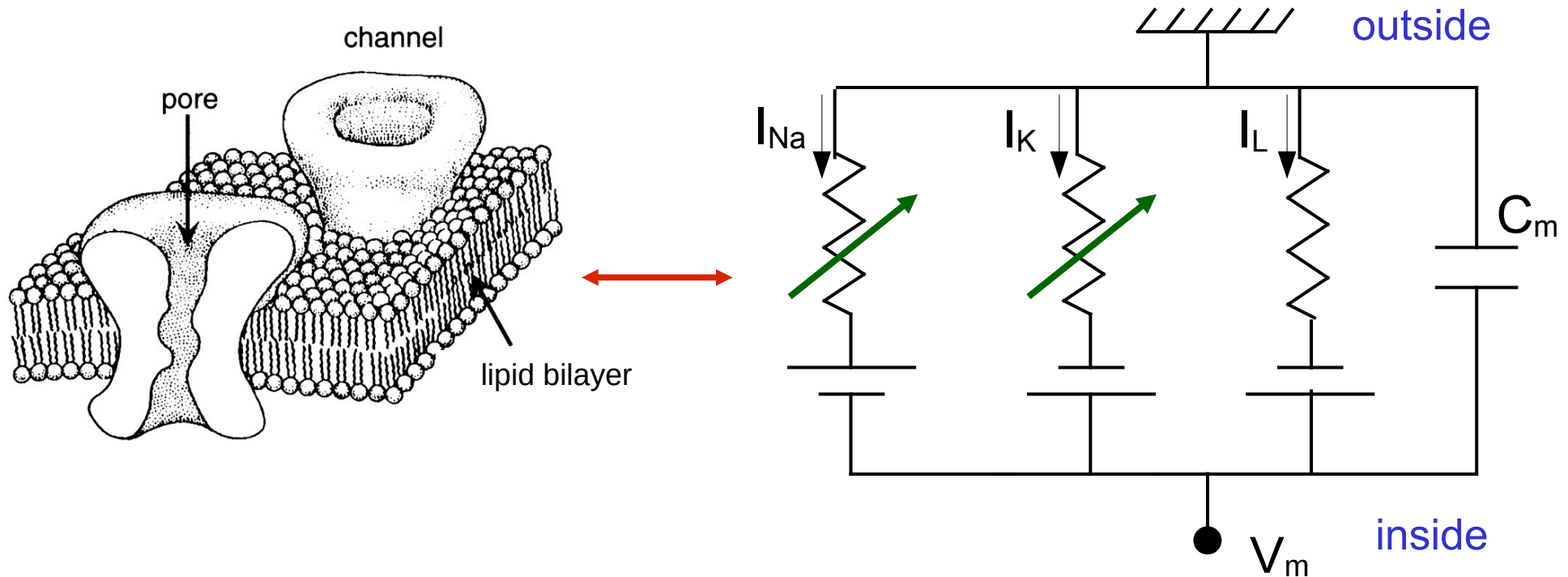
$$I = \frac{V}{R} \qquad R = \frac{1}{g}$$

Kirchoff's law :

The sum of currents flowing into a point is equal to the sum of currents flowing out of that point..

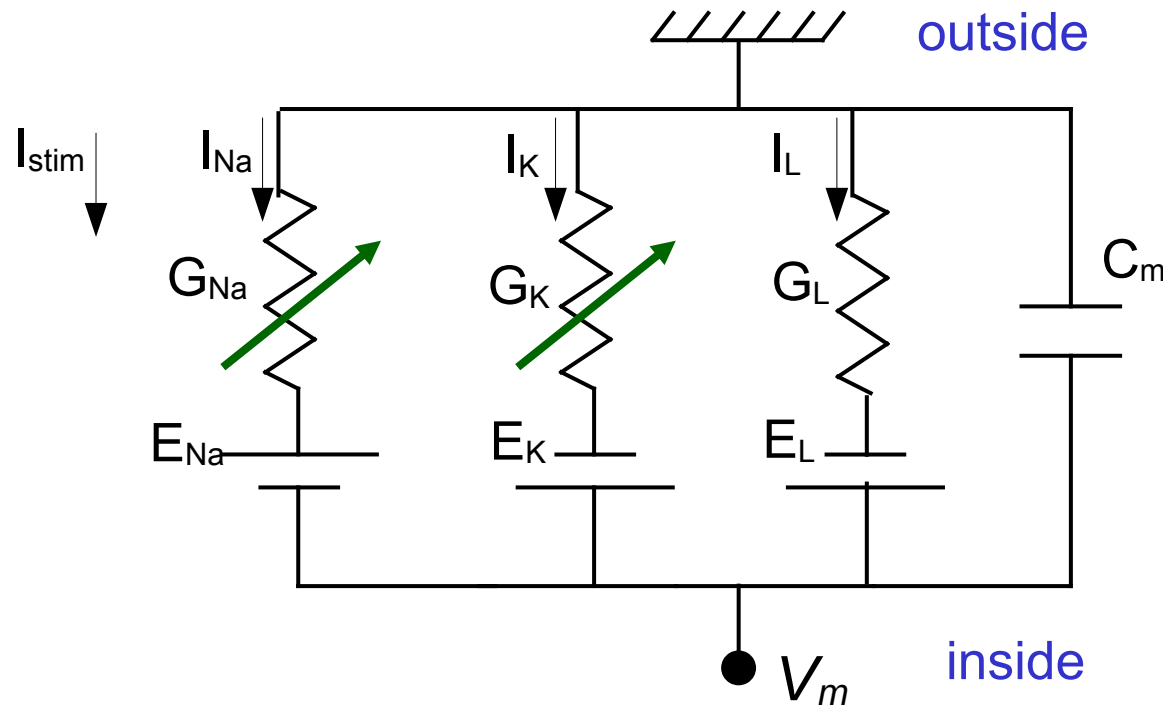
$$I_1 + I_2 + I_3 + \dots = 0$$

Membrane properties : equivalent circuit



- The membrane potential V_m varies due to the opening/closing of different types of ion channels.
- “**Active membrane**” : Ion channel conductance varies with the membrane potential.

Hodgkin-Huxley model : membrane potential equation



Kirchhoff's law :

$$I_{stim} = I_{Na} + I_K + I_L + I_C$$

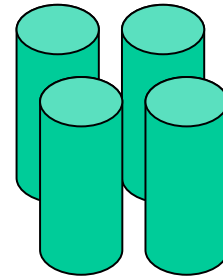
Ohm's law :

$$R = \frac{\Delta V}{I} \rightarrow I = \frac{\Delta V}{R} = g(V_m - V_{rev})$$

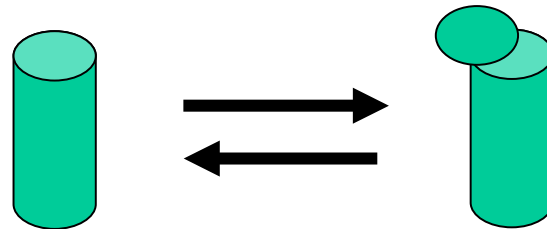
$$\rightarrow I_{stim} = g_{Na}(t)(V_m - V_{Na}) + g_K(t)(V_m - V_K) + g_L(V_m - V_L) + C \frac{dV_m}{dt}$$

Hodgkin-Huxley model : potassium channel

→ 4 similar sub-units



→ Each subunit can be « open » or « closed » :



→ The channel is « open » if and only if all the sub-units are « open »

Hodgkin-Huxley model : potassium channel

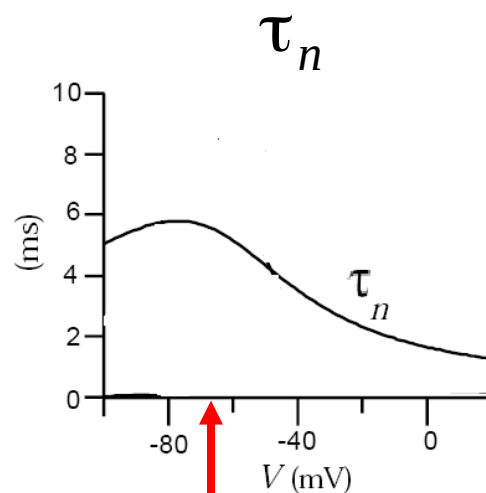
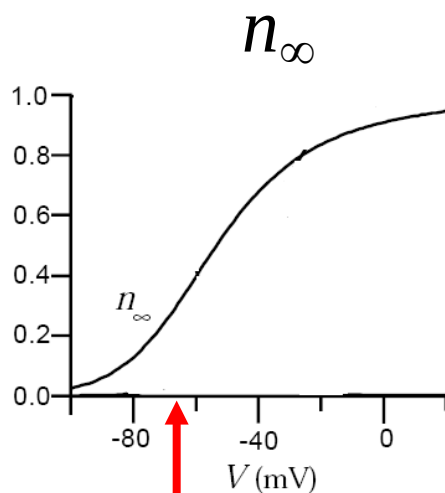
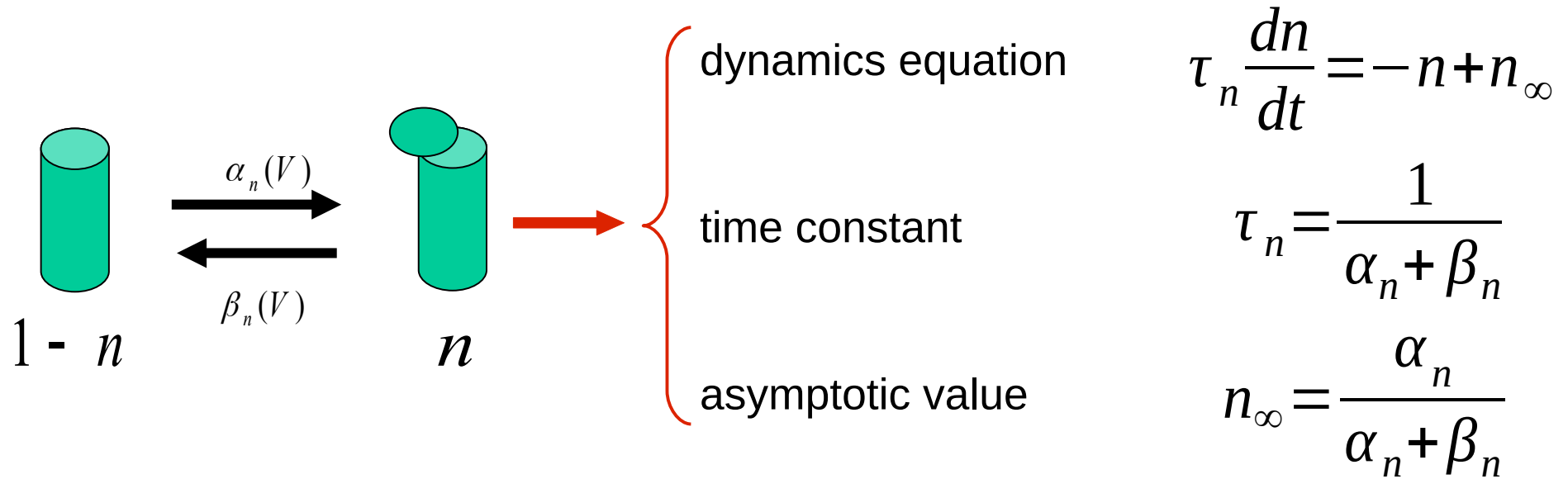
- probability that one sub-unit is « open » : $n(t)$
- probability that all sub-units are « open » : $n(t)^4$
- maximal K⁺ conductance, when all channels are open : $\bar{g}_K$
- K⁺ conductance : $g_k = \bar{g}_K n(t)^4$

$$C \frac{dV}{dt} = g_{Na}(t)(V_{Na} - V) + g_K(t)(V_K - V) + g_L(V_L - V) + I_{stim}$$



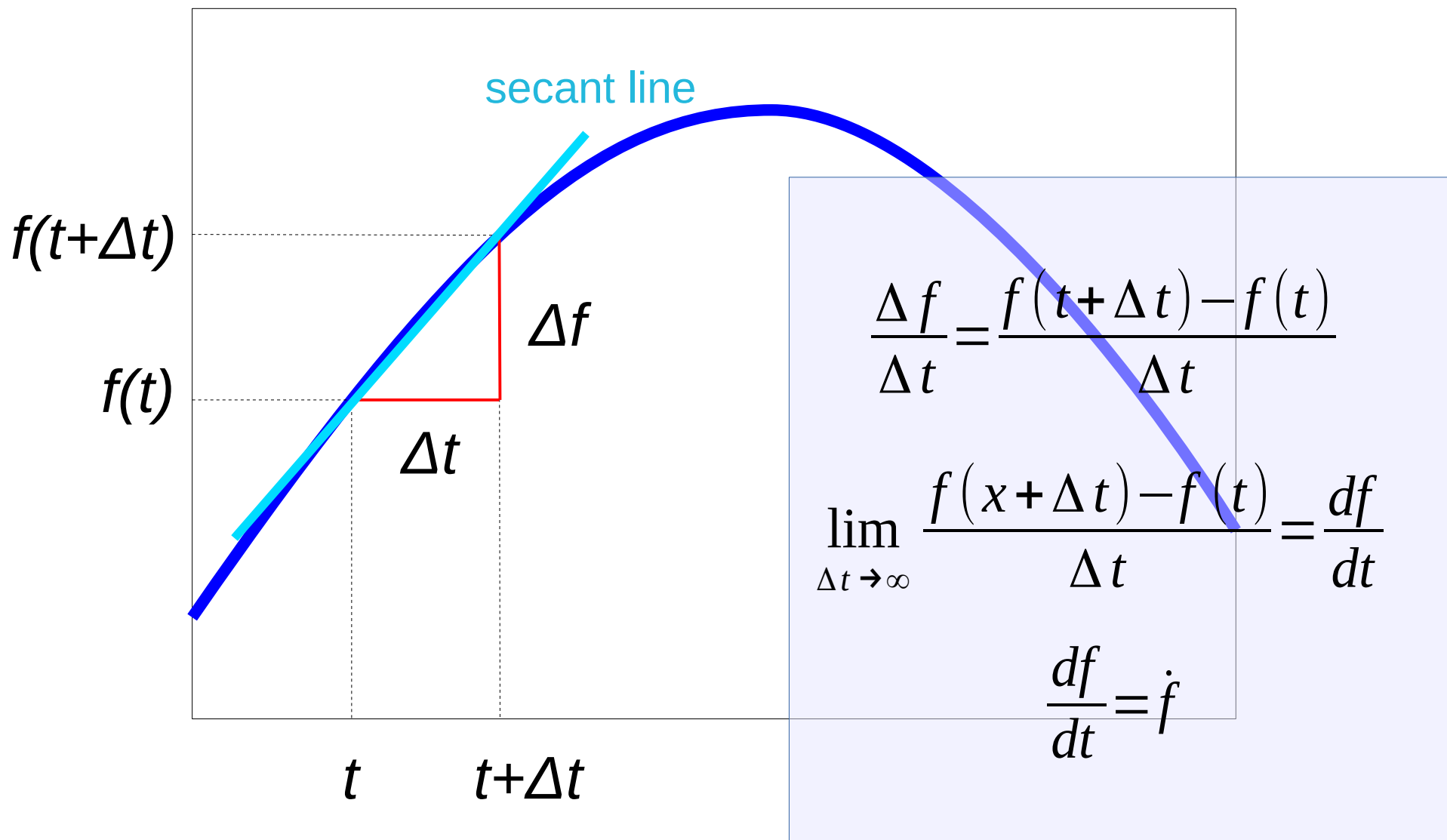
$$C \frac{dV}{dt} = g_{Na}(t)(V_{Na} - V) + \bar{g}_K n(t)^4 (V_K - V) + g_L(V_L - V) + I_{stim}$$

Hodgkin-Huxley model : potassium channel



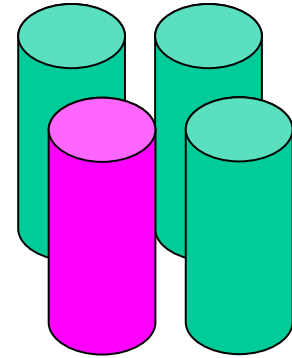
→ The potassium channel is closed at resting potential.

Math reminder : difference quotient

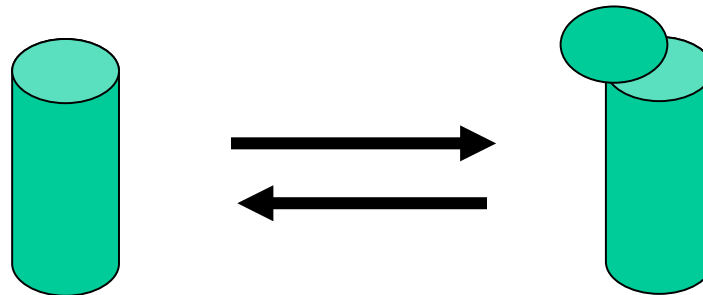


Hodgkin-Huxley model : sodium channel

- The sodium channel has 3 similar « fast » esub-units and 1 « slow » subunit



- Each sub-unit can be « open » or « closed »



- The channel is « open » if and only if all the sub-units are « open »

Hodgkin-Huxley model : sodium channel

- Probability that the « fast » sub-unit is « open » : m
- Probability that the « slow » sub-unit is « open » : h
- Probability that the channel is « open » : $m^3 h$
- Maximal Na⁺ conductance, when all channels are open : $\bar{g}_{Na}$
- Na⁺ conductance : $g_{Na} = \bar{g}_{Na} m^3 h$

$$C \frac{dV}{dt} = g_{Na} (V_{Na} - V) + g_K (V_K - V) + g_L (V_L - V) + I_{ext}$$



$$C \frac{dV}{dt} = \bar{g}_{Na} m^3 h (V_{Na} - V) + \bar{g}_K n^4 (V_K - V) + g_L (V_L - V) + I_{stim}$$

Hodgkin-Huxley model : sodium channel

dynamics of the fast sub-unit

$$\tau_m \frac{dm}{dt} = -m + m_\infty$$

$$\tau_m = \frac{1}{\alpha_m + \beta_m}$$

$$m_\infty = \frac{\alpha_m}{\alpha_m + \beta_m}$$

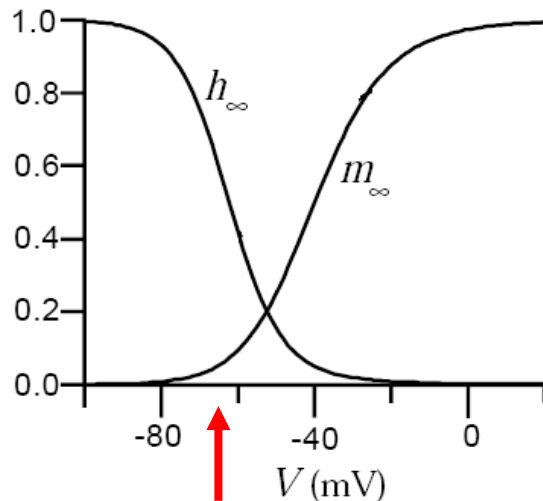
dynamics of the slow sub-unit :

$$\tau_h \frac{dh}{dt} = -h + h_\infty$$

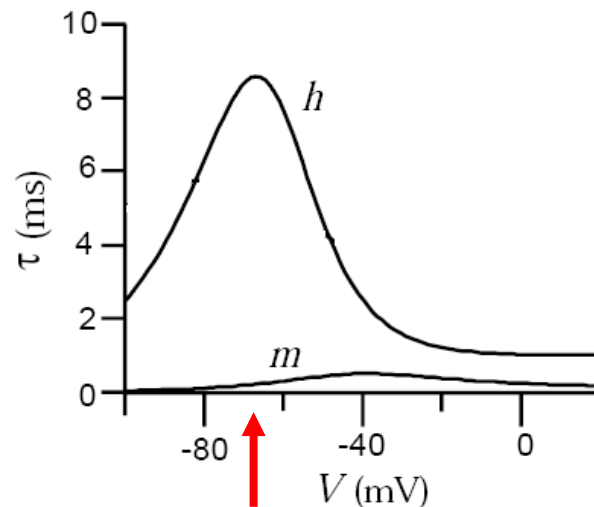
$$\tau_h = \frac{1}{\alpha_h + \beta_h}$$

$$h_\infty = \frac{\alpha_h}{\alpha_h + \beta_h}$$

asymptotic values



time constants



- The fast sub-unit is closed at resting potential.
- The slow sub-unit is open at resting potential.
- The sodium channel is closed at resting potential.

Complete equations of the Hodgkin-Huxley model

$$C \frac{dV}{dt} = \bar{g}_{Na} m^3 h (V_{Na} - V) + \bar{g}_K n^4 (V_K - V) + g_L (V_L - V) + I_{stim}$$

$$\tau_n \frac{dn}{dt} = -n + n_\infty, \tau_n = \frac{1}{\alpha_n + \beta_n}, n_\infty = \frac{\alpha_n}{\alpha_n + \beta_n}$$

$$\tau_m \frac{dm}{dt} = -m + m_\infty, \tau_m = \frac{1}{\alpha_m + \beta_m}, m_\infty = \frac{\alpha_m}{\alpha_m + \beta_m}$$

$$\tau_h \frac{dh}{dt} = -h + h_\infty, \tau_h = \frac{1}{\alpha_h + \beta_h}, h_\infty = \frac{\alpha_h}{\alpha_h + \beta_h}$$

$$\alpha_n(V) = \frac{(0.1 - 0.01V)}{e^{1-0.1V} - 1}$$

$$\alpha_m(V) = \frac{(2.5 - 0.1V)}{e^{2.5-0.1V} - 1}$$

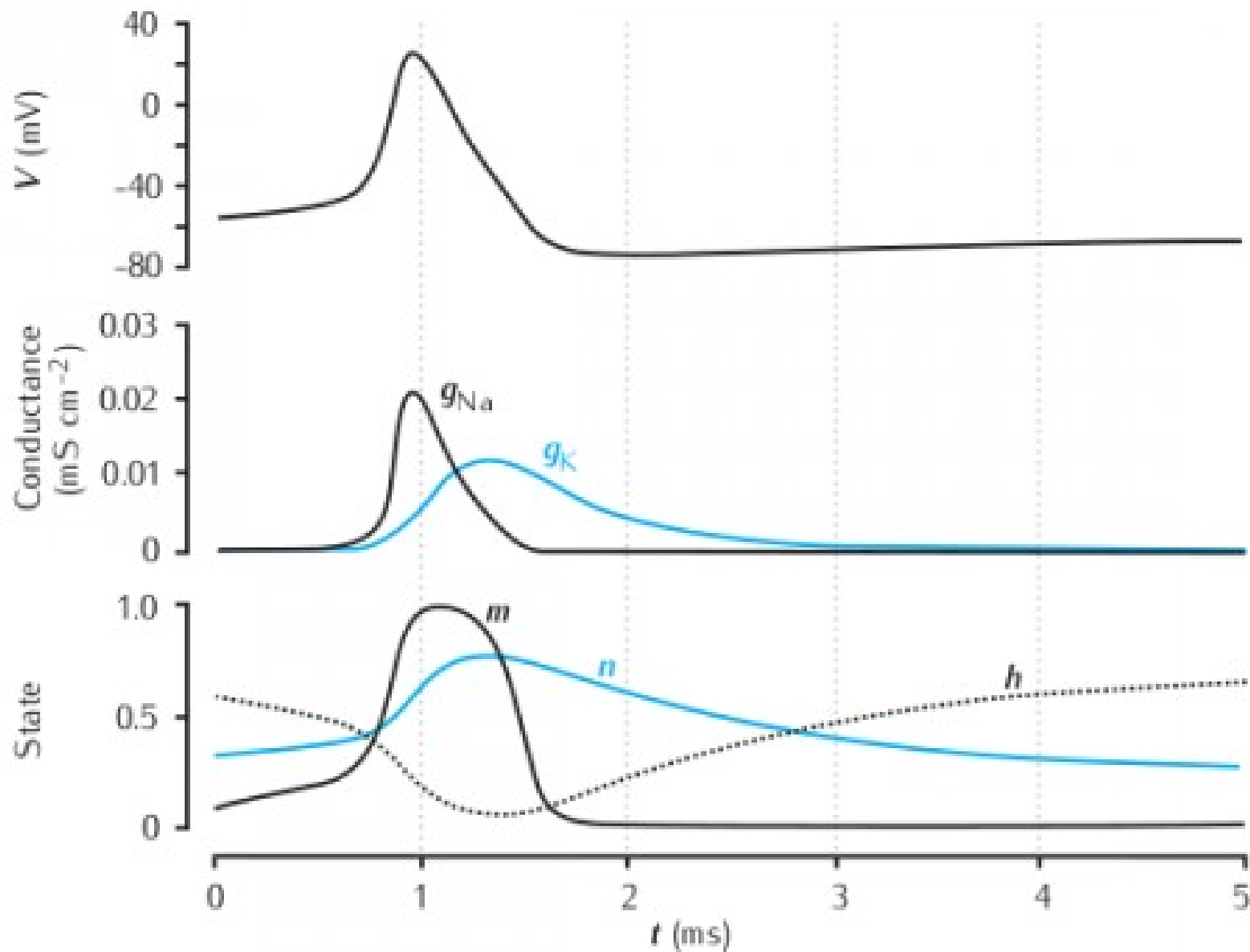
$$\alpha_h(V) = 0.07 e^{-\frac{V}{20}}$$

$$\beta_n(V) = 0.125 e^{-\frac{V}{80}}$$

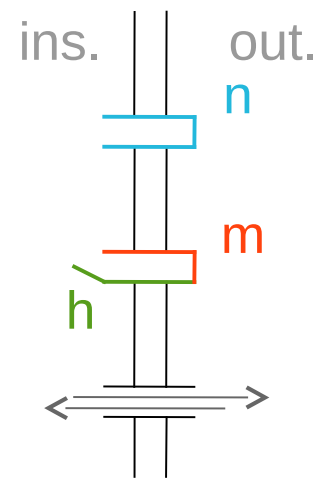
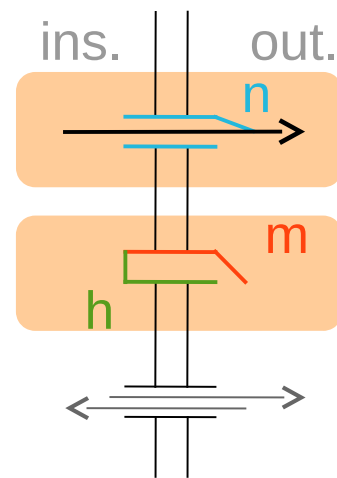
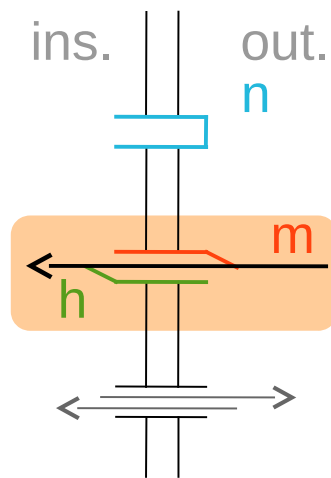
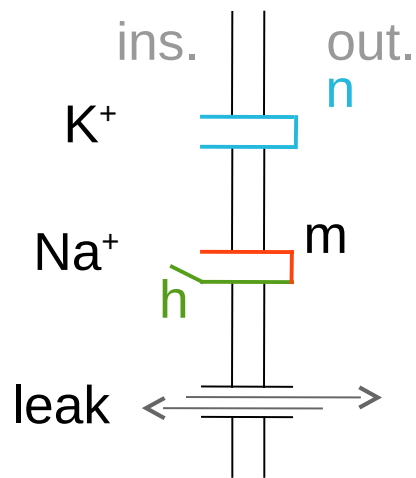
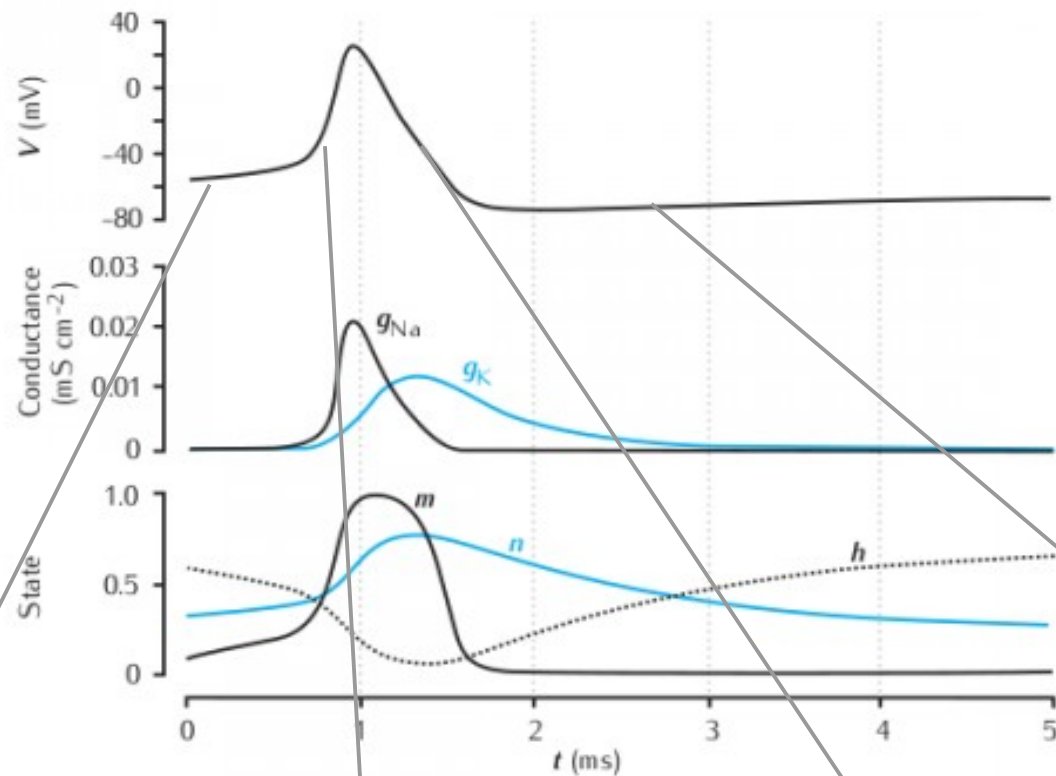
$$\beta_m(V) = 4 e^{-\frac{V}{18}}$$

$$\beta_h(V) = \frac{1}{e^{3-0.1V} + 1}$$

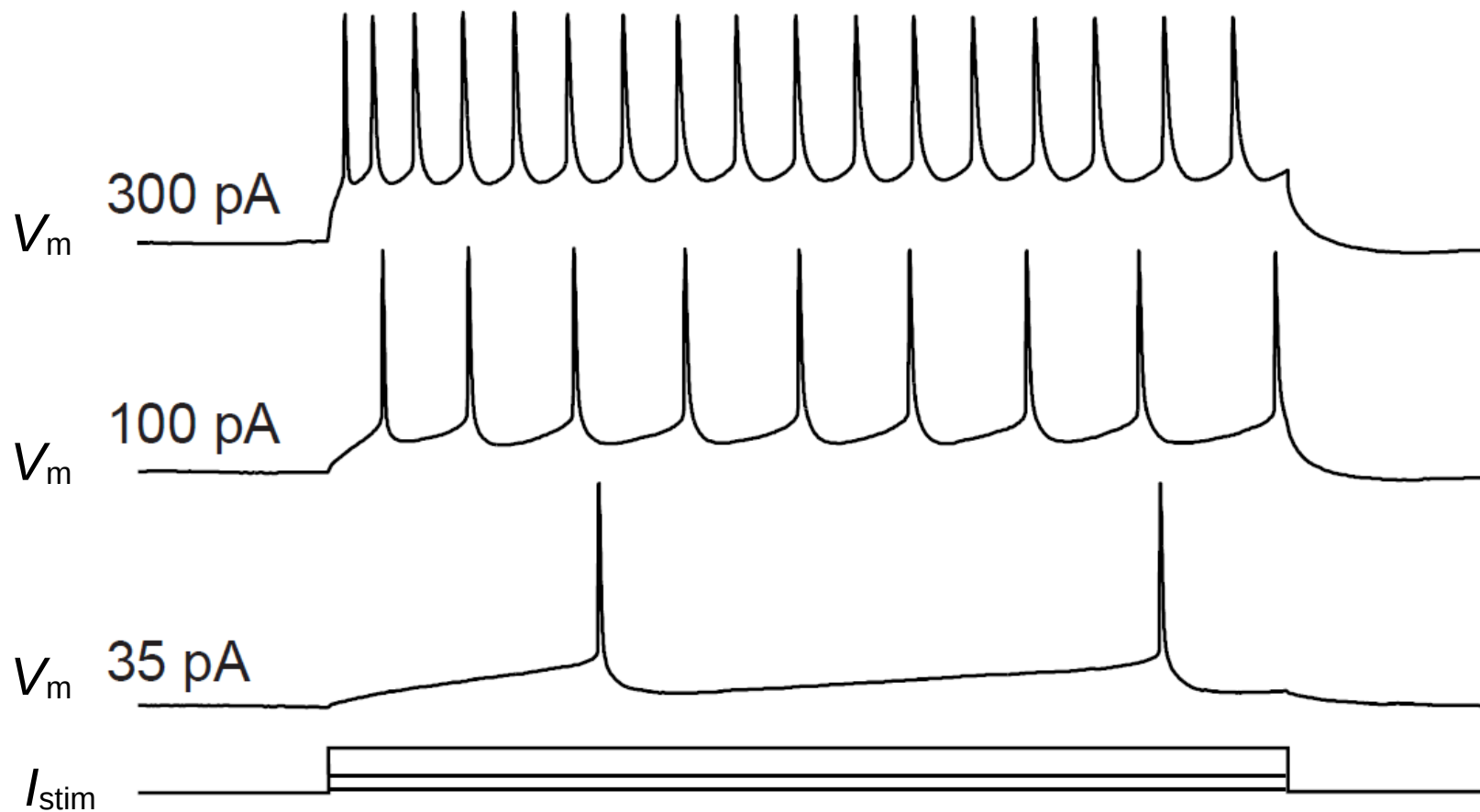
Hodgkin-Huxley model : the action potential



Hodgkin-Huxley model : the action potential

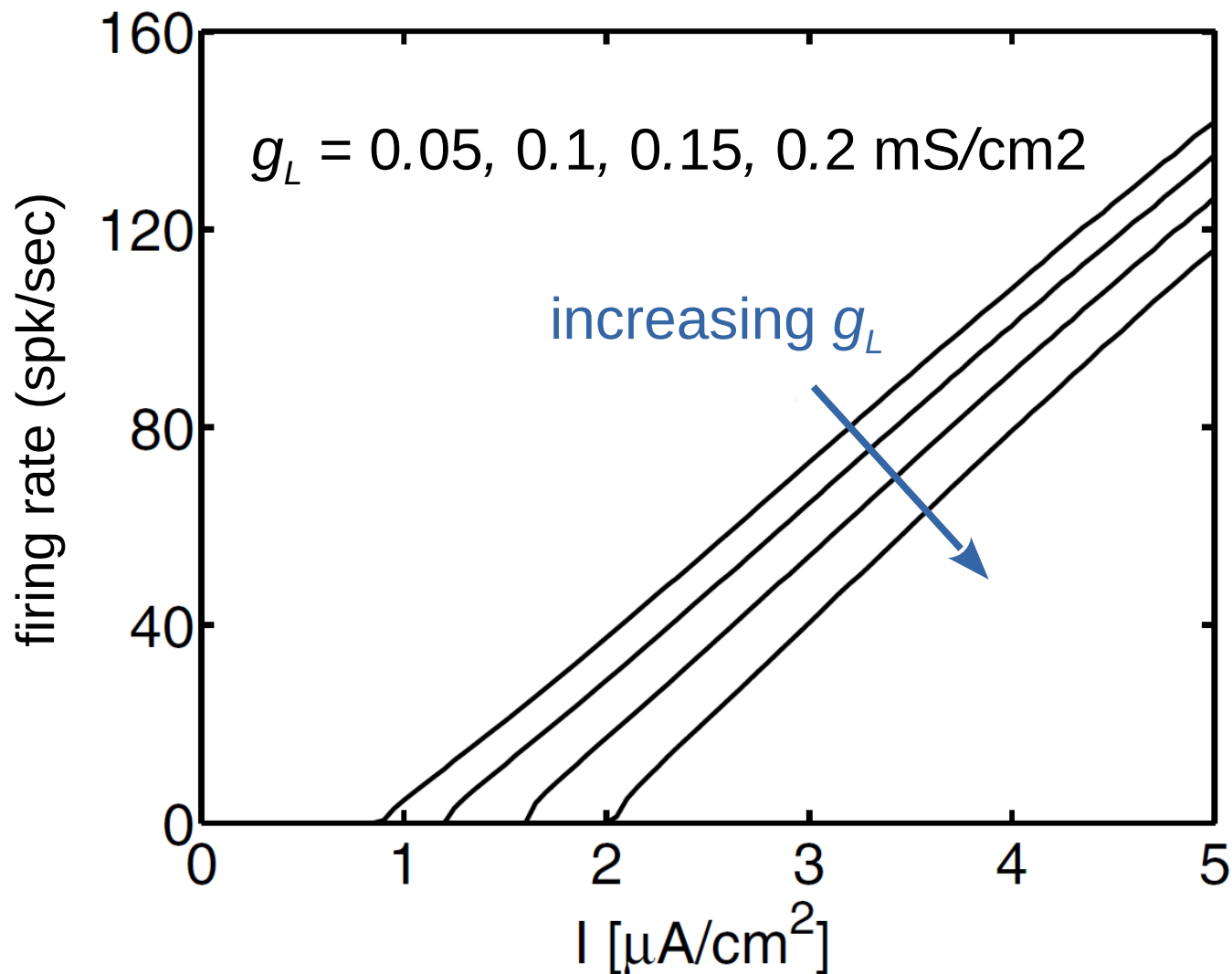


Hodgkin-Huxley model : current injection

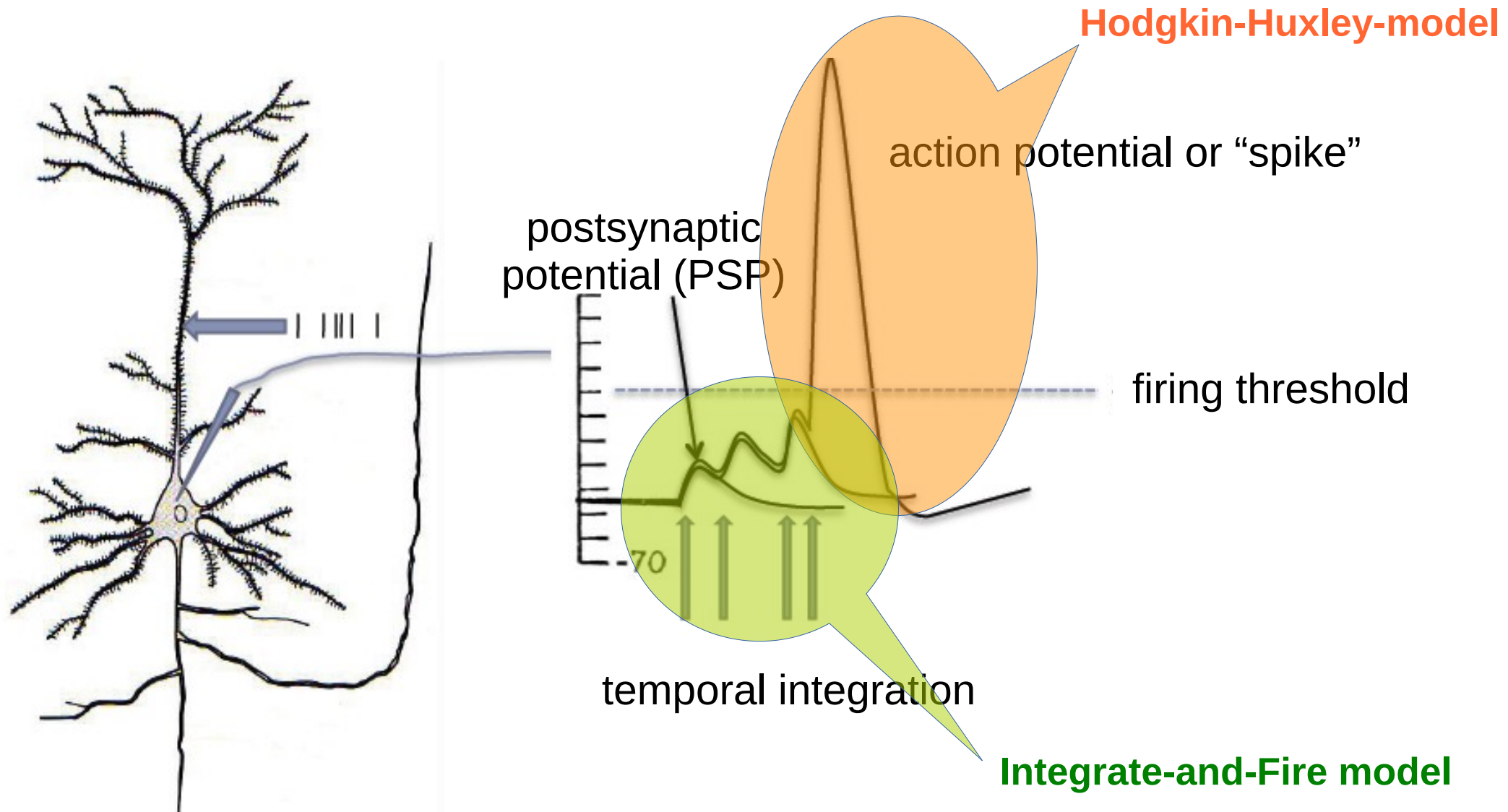


Hodgkin-Huxley model : F-I curve

Example : study the role of the membrane permeability (conductance g_L) on action potential output



Neural integration



Integrate-and-Fire model : derivation

simplification : no active currents $\longrightarrow g(t) = \text{const.}$

→ The shape of the action potential is not described !

$$C \frac{dV}{dt} = g_{Na} (V_{Na} - V) + g_K (V_K - V) + g_L (V_L - V) + I_{stim}$$

$$C \frac{dV}{dt} = \underbrace{g_{Na} V_{Na} + g_K V_K + g_L V_L}_{G_{tot}} - \underbrace{(g_{Na} + g_K + g_L)}_{G_{tot}} V + I_{stim}$$

$$C \frac{dV}{dt} = G_{tot} (V_0 - V) + I_{stim}$$

$$\tau = \frac{C}{G_{tot}}$$

$$\tau \frac{dV}{dt} = (V_0 - V) + \frac{I_{stim}}{G_{tot}}$$

Integrate-and-Fire model : membrane potential equation

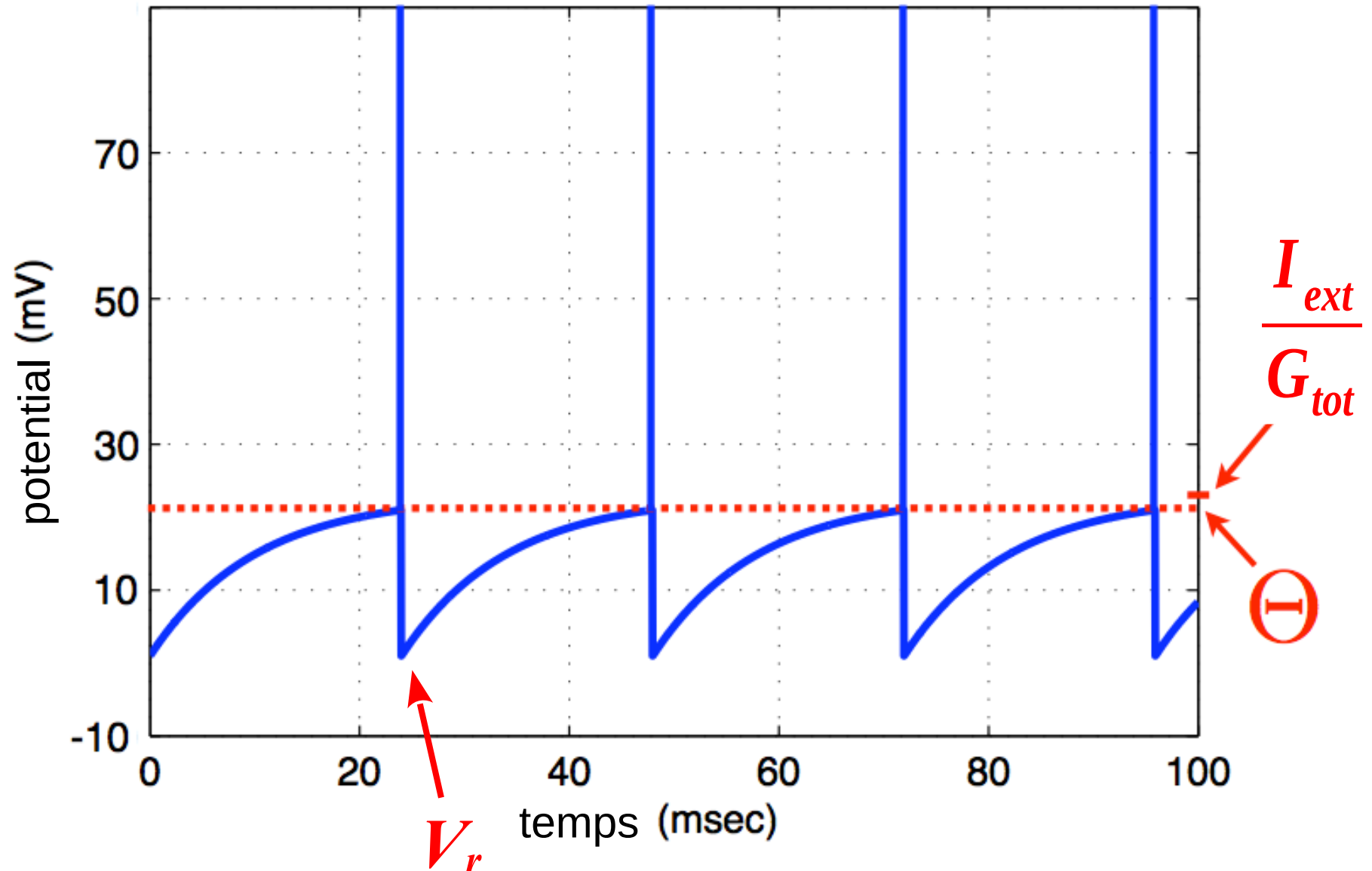
$$\tau \frac{dV}{dt} = (V_0 - V) + \frac{I_{ext}}{G_{tot}}$$

- V_0 resting membrane potential
- τ membrane time constant
- I_{ext} external current (synaptic)
- G_{tot} total conductance

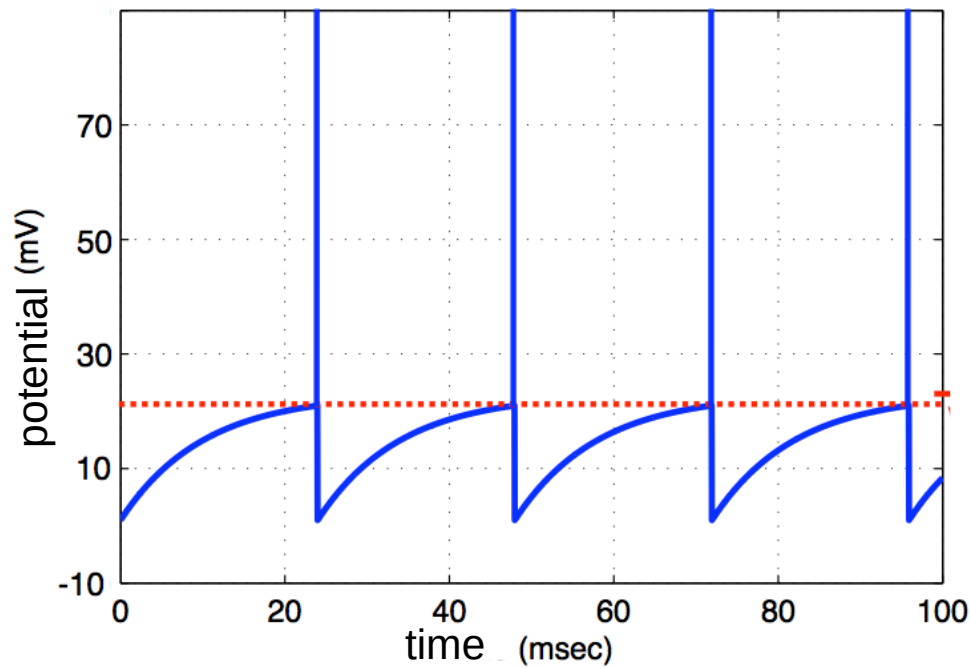
generation of the action potential :

- Θ firing threshold
- V_r reset potential
- if $V > \Theta$:
 - the neuron fires an action potential
 - after the action potential, the membrane potential is reset to V_r

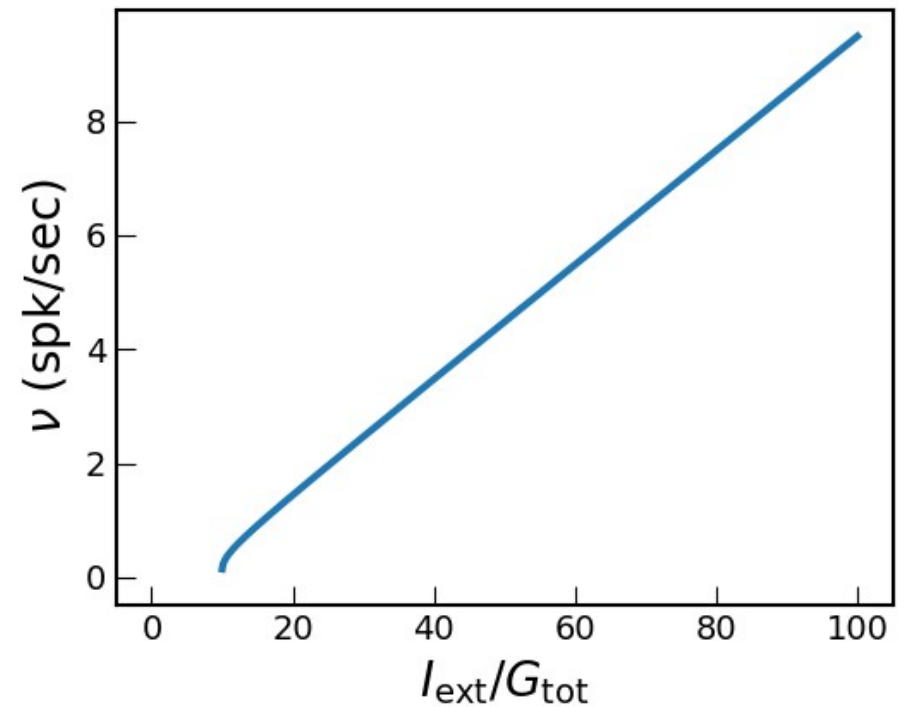
Integrate-and-Fire model : dynamics



Integrate-and-Fire model : dynamics

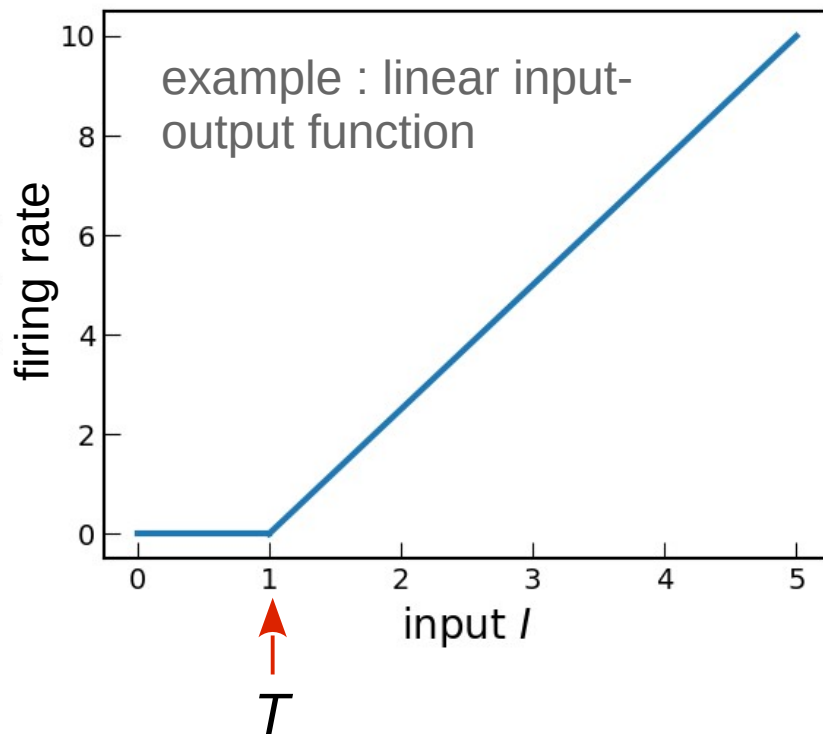


F-I curve



Rate neuron model

Phenomenological description of the input-output function :



$$\tau \frac{dm}{dt} = -m + F(I_{syn} + I_{ext} - T)$$

m: output of the neuron – firing rate

τ : membrane time constant

F : input-output transfer function

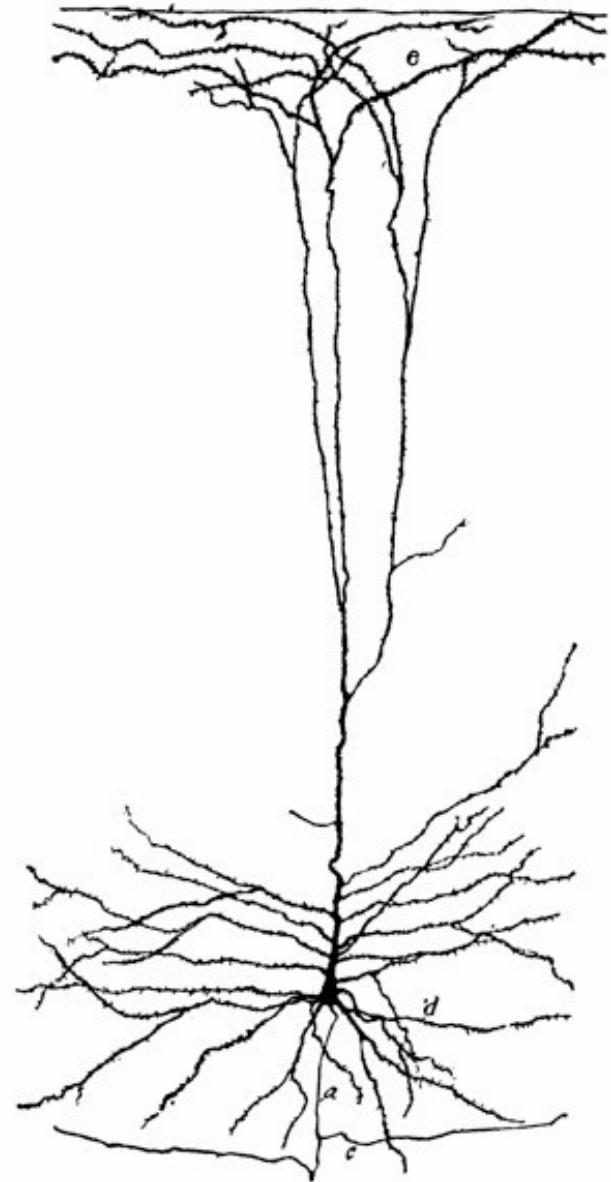
I_{syn}: synaptic input

I_{ext}: external current

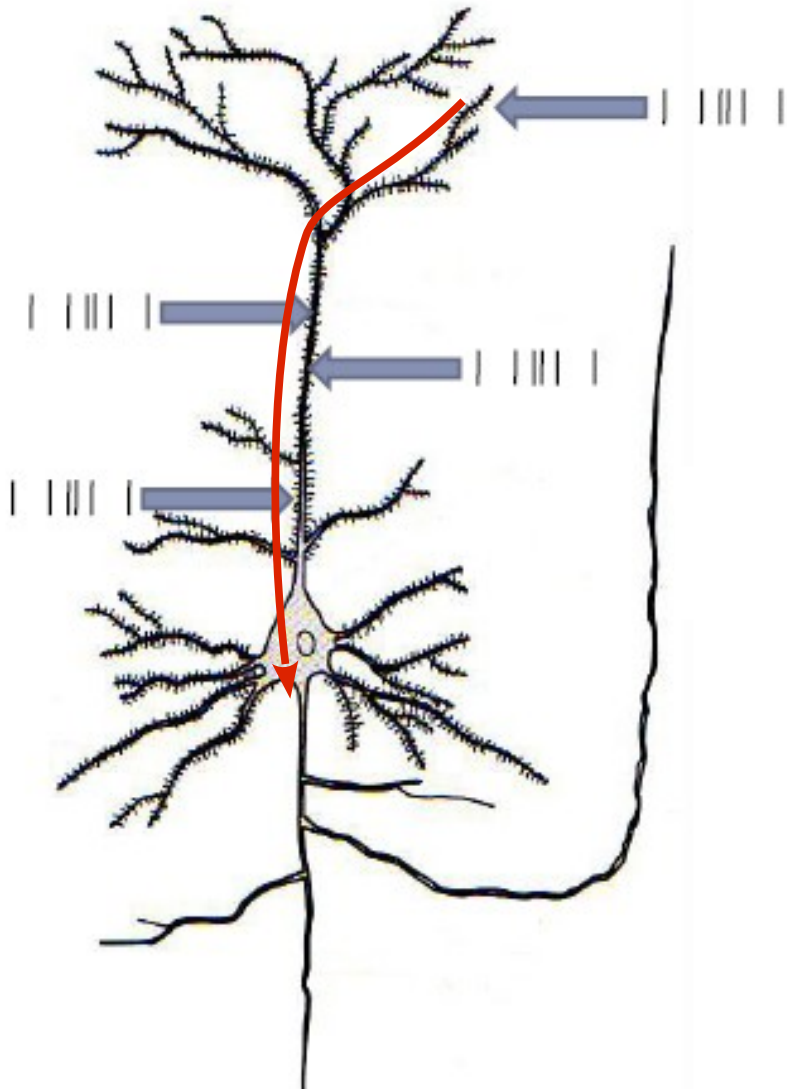
T : firing threshold

How do potentials propagate along the dendritic tree ?

$V(t)$

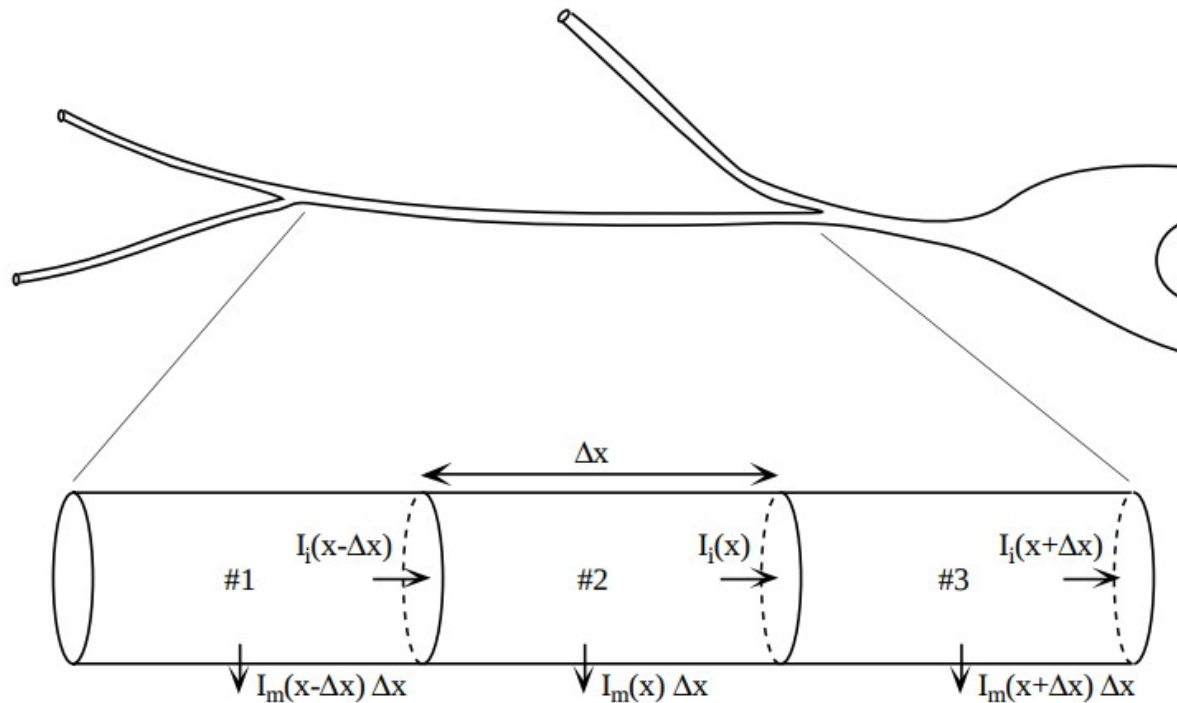


Cable theory



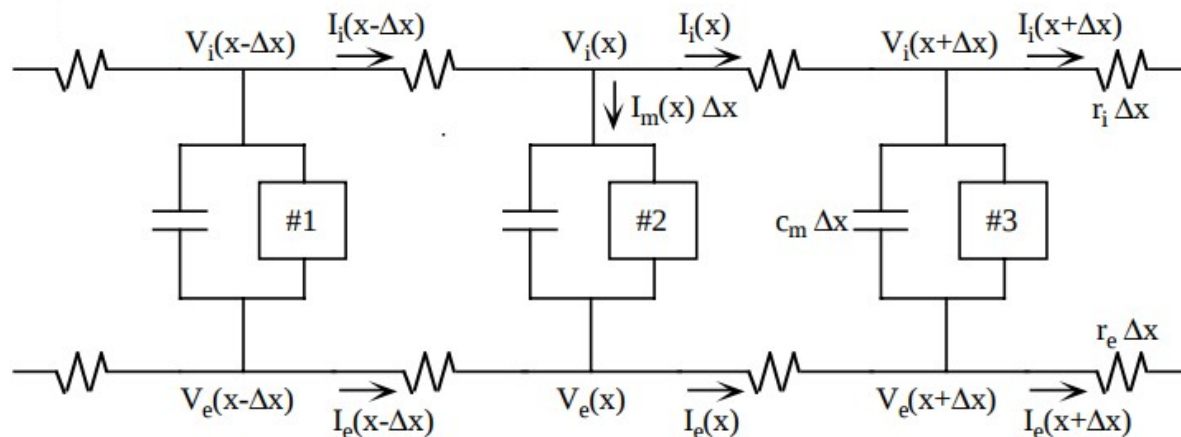
- how do synaptic inputs propagate to the soma or the axon initial segment
- how do input interact between each other
- how does the input location along the dendritic tree impact its functional importance for the neuron

Abstraction of the dendritic membrane of a neuron



Soma and dendritic branch

Portion of the secondary dendrite divided in three sub-cylinders



Discrete electric model of the three sub-cylinders

Non-linear cable equation

models the membrane potential distribution along a membrane cylinder

$$V(t) \rightarrow V(x,t)$$

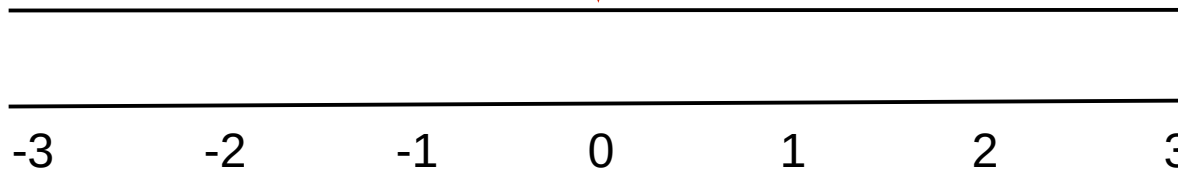
$$\frac{1}{r_i + r_e} \frac{\partial V}{\partial x^2} = c_m \frac{\partial V}{\partial t} + I_{ion}$$

current which propagates
between neighboring points
along the cylinder

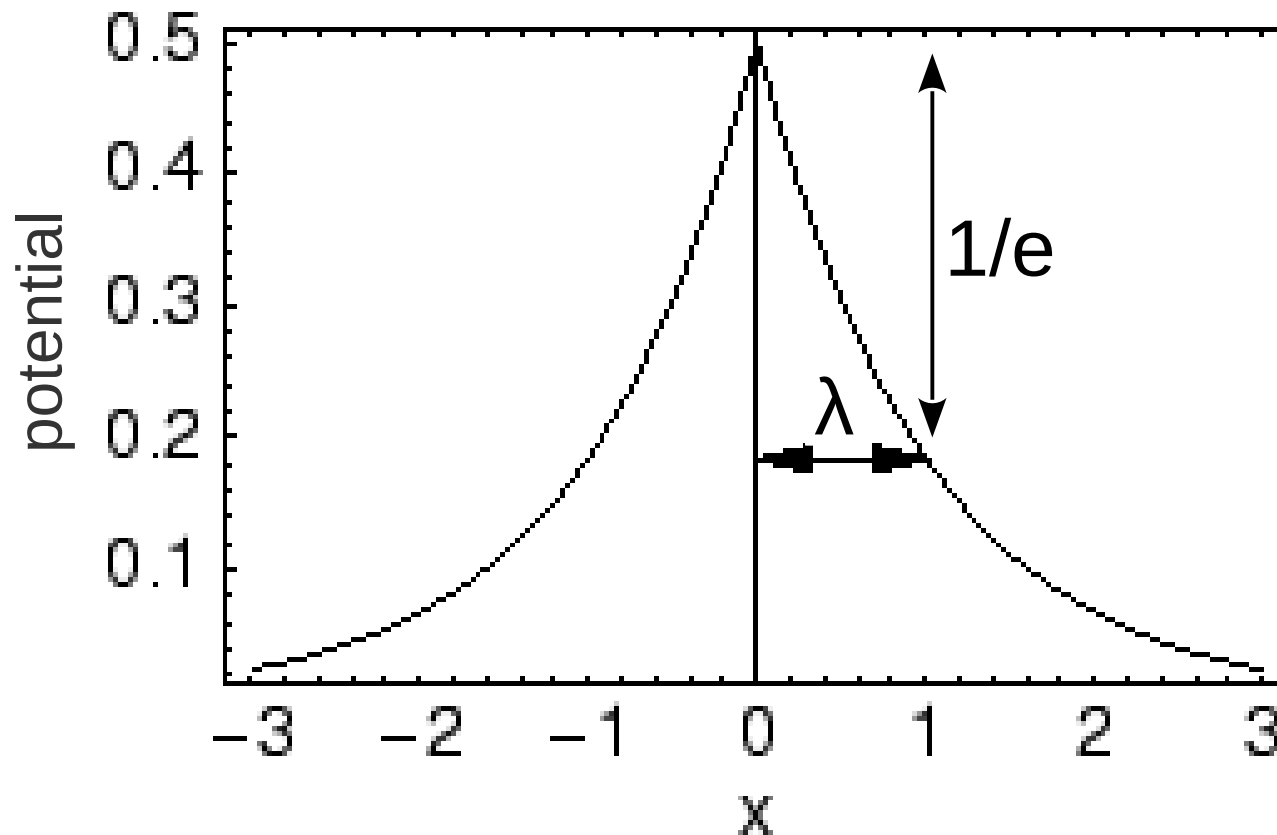
typical membrane potential
equation of the point neuron
model

Stationary solution of the cable equation

$$\downarrow I_{ext}(t, x) = \delta(x)$$

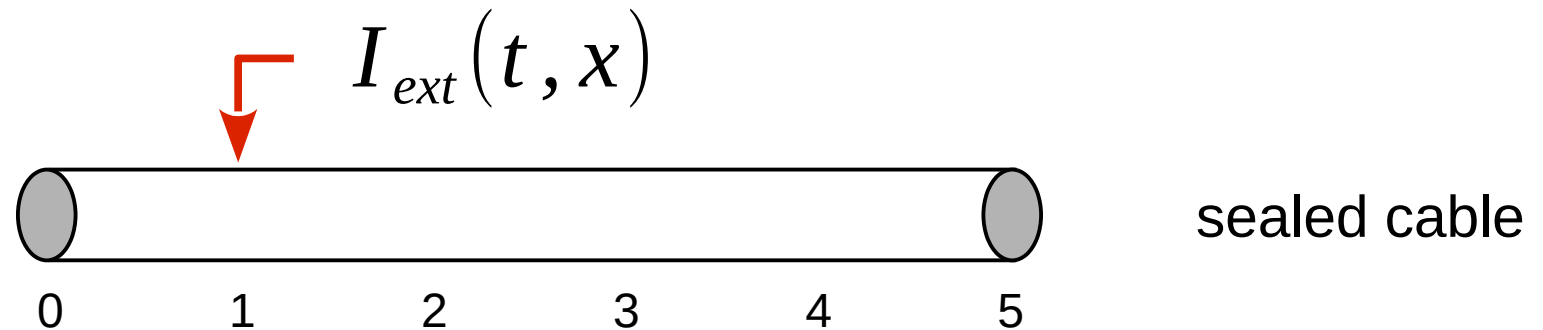


infinite cable
(open ends)

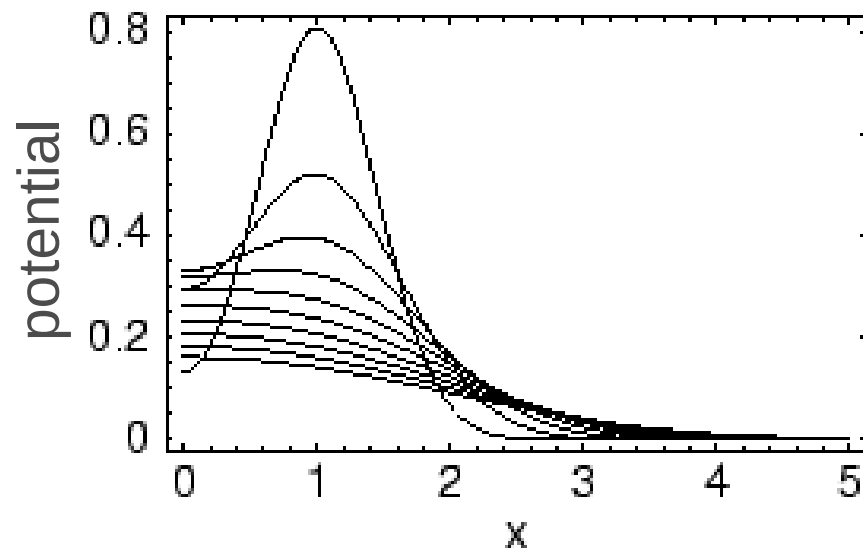


λ electrotonic
length constant

Spatial and temporal distribution of the potential along the membrane

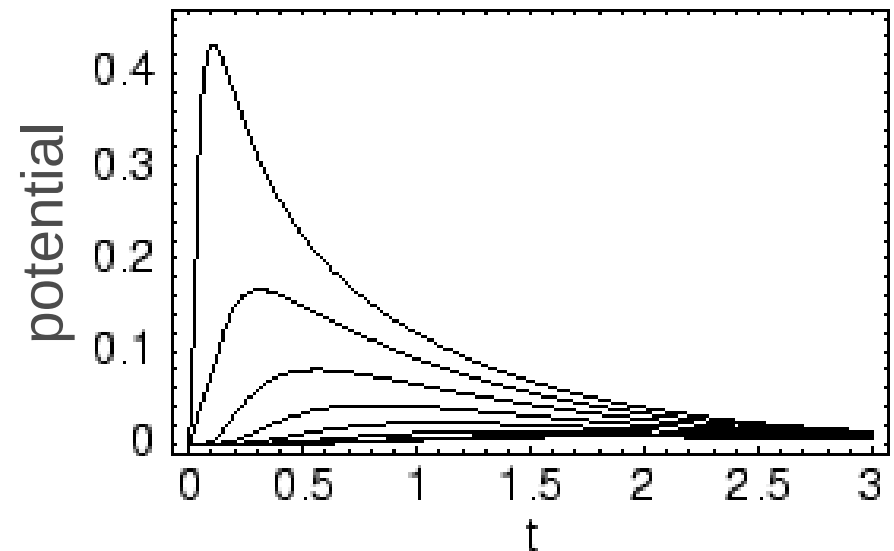


different time points



$t = 0.1, 0.2, \dots, 1.0$

different locations



$x = 1.5, 2.0, 2.5, \dots, 5.0$

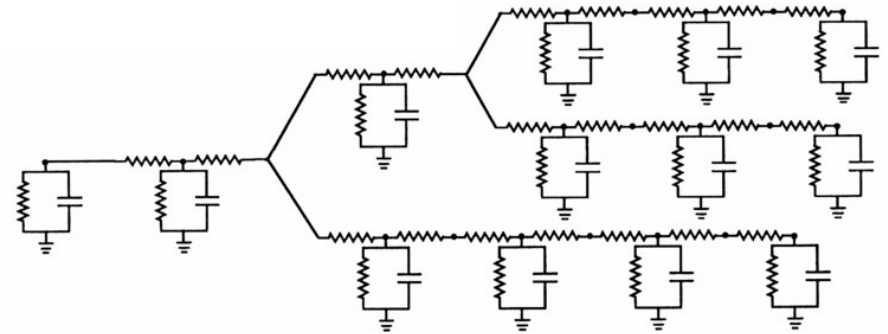
Cable theory and compartmental modeling

Cable theory consists of solving the partial differential equation

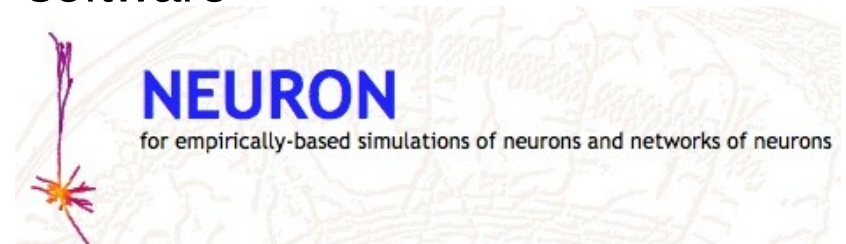
$$\frac{1}{r_i + r_e} \frac{\partial V}{\partial x^2} = c_m \frac{\partial V}{\partial t} + I_{ion}$$

- a few cases with analytical solutions
- generally solved using numerical simulations

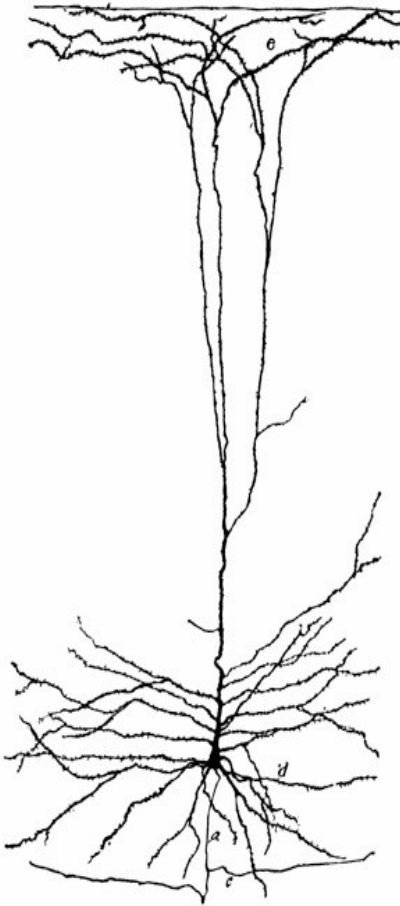
Compartmental modeling



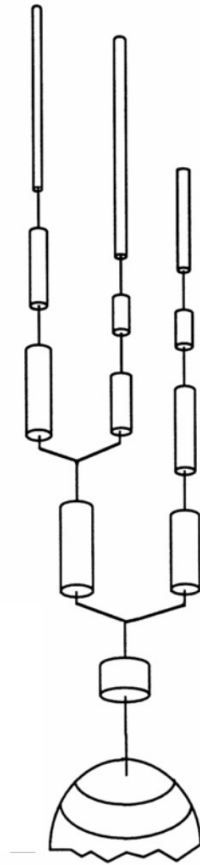
- discretize space → coupled system of ordinary differential equations (with temporal derivative)
- easier to solve numerically
- typically done using the Neuron software



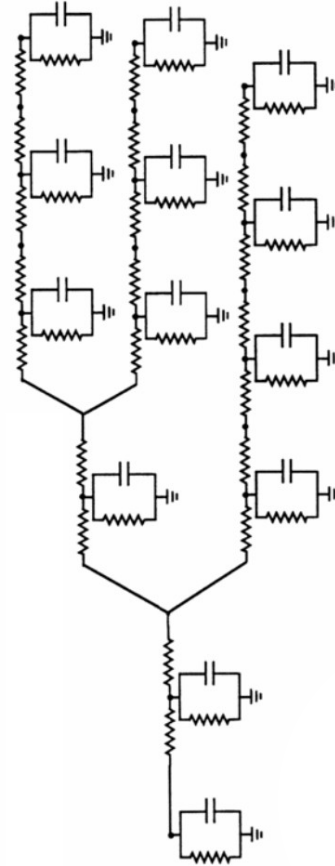
Single neuron models



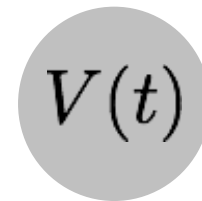
real
neuron



cable
theory

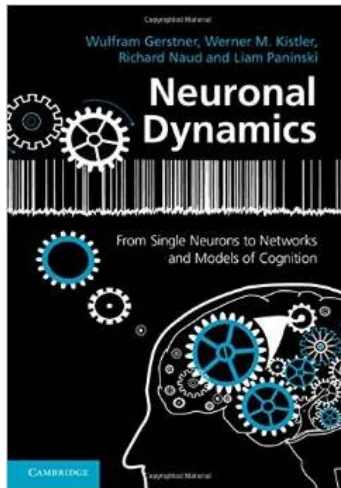


compartmental
model



point
neuron

Resources for further reading

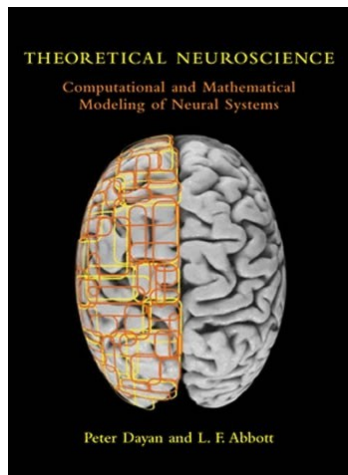


Neuronal Dynamics

From single neurons to networks and models of cognition

Wulfram Gerstner, Werner M. Kistler, Richard Naud and Liam Paninski

online book : <https://neurondynamics.epfl.ch/online/index.html>



Theoretical Neuroscience

Computational and Mathematical Modeling of Neural Systems

Peter Dayan and L. F. Abbott

online book : <http://www.gatsby.ucl.ac.uk/~limate/biblio/dayanabbott.pdf>